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AN ANALYSIS OF PEPTIC ULCER IN SOUTH AUSTRALIA, BASED ON A STUDY OF 1,027 CASE REPORTS.

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PEPTIC ULCER is a very old disease. Characteristic symptoms were mentioned by Hippocrates in the fourth century before Christ. He said: "Blood discharged upwards, whatever be its character, is a bad symptom, but downward is more favourable, and so also black dejections." A little later he wrote: "When the liver is filled with water and bursts into the epiploon, in this case the belly is filled with water and the patient dies." This latter is probably the description of a ruptured ulcer. These symptoms have been known for many years, but it was not until late in the eighteenth century that their underlying pathology began to be understood. In 1793 Matthew Baillie first described the pathology of gastric ulcer, but he gave no clinical data. The credit of being the first to recognize the difference between ulcer of the stomach, carcinoma and ordinary gastritis probably belongs to Cruveilhier, who between 1829 and 1835 published accurate descriptions of the anatomy, the clinical course and the treatment of peptic ulcer. From then on medical literature abounds in articles upon this disease. However, very few of these have materially advanced our knowledge of the pathology of the condition.

A great many theories have been advanced regarding the initial cause of peptic ulcer, including the inflammatory, neurogenic, circulatory, bacterial and digestive or corrosive theories. Today two of the most widely held are the nutritional and psychogenic theories; but the true pathogenesis of this condition has not yet been established.

From a perusal of the literature on peptic ulcer it is clear that considerable variation in both incidence and symptomatology occurs in different countries and even in cities of the same country. Hence it is necessary to make a statistical survey of this condition in each large centre of population. In view of this an investigation was undertaken in Adelaide, and the case notes of patients admitted to the Royal Adelaide Hospital during the years 1939 to 1944 inclusive were used for this purpose. Over 2,000 case notes of patients with suspected peptic ulcer were perused, but only those with the following findings were used for this series: (i) an ulcer found at operation; (ii) an ulcer niche seen in the X-ray film; (iii) a typical history of pain with suggestive X-ray findings and the finding of occult blood in the faeces or the occurrence of gross hæmorrhage.

There were 1,027 such cases. In the majority investigations were made to exclude pulmonary tuberculosis and cholecystitis. Thus only cases in which a reasonably accurate diagnosis of peptic ulcer had been made were used in this investigation. The only exception to this was in cases of acute erosion of the stomach and duodenum. Nearly all of these patients had a sudden gross hæmorrhage, and in the X-ray investigation of many some irregularity of function was found.

Of the 953 chronic ulcers (including ruptured ulcers), 357 (37.5%) were gastric and 565 (59.3%) were duodenal. The remaining 31 cases were comprised of 20 (2.1%) in which gastric and duodenal ulcer occurred together, and 11 (1.1%) in which a stomal ulcer was present. Thus duodenal ulcer outnumbered gastric ulcer in the proportion of 3 to 2, and the sex ratio is about 7 to 1 in favour of males in both instances (Table I).

ANNUAL ADMISSIONS BY AGE AND SEX GROUPS.

Chronic Peptic Ulcer.

There were 763 cases in the group comprising chronic peptic ulcer (not ruptured). In the case of both gastric

ulcer and duodenal ulcer the age incidence for females was found to be much the same as that for males. However, the maximum incidence of gastric ulcer is in subjects aged between forty and fifty-nine years, over one-half being between these ages. On the other hand, the incidence of duodenal ulcer falls much more in the twenty to thirty-nine years age group, although the maximum incidence is still within the forty to fifty-nine years group. The sixty years and over group contained a considerably smaller number of cases of duodenal ulcer than of gastric

gastric ulcer and 57 had duodenal ulcer. This is a proportion of 2:1 in favour of gastric ulcer. Another striking fact discovered was that in cases of gastric ulcer the ratio of males to females was 19.4:1, while in cases of duodenal ulcer it was still higher at 27.6:1. Only one ruptured ulcer occurred in a subject aged under twenty years, and the maximum age incidence was much the same as for chronic unruptured ulcers—that is, in the forty to fifty-nine year group for both gastric ulcer and duodenal ulcer. However, a larger number of cases of duodenal ulcer occurred in the twenty to thirty-nine year group (Table III).

TABLE I.

Summary of Admissions to Hospital for Chronic Peptic Ulcer (Including Ruptured Ulcer).

Type of Ulcer.	Total Patients.	Male.	Female.	Ratio Males to Females. ¹
Gastric	357	310	47	6.6
Duodenal	565	497	68	7.3
Ratio D/G ² ..	1.6	1.6	1.4	(1.1)

¹ Ratio for sexes gives figure for males, that for females being regarded as unity.

² Ratio for duodenal ulcers and gastric ulcers gives figure for duodenal ulcers, that for gastric ulcers being regarded as unity.

ulcer, so it is evident that duodenal ulcer is a disease which occurs in a younger set of people than gastric ulcer. Nearly 70% of patients with duodenal ulcer were aged over forty years, while 85% of patients with gastric ulcer were over this age (Table II).

Ruptured Ulcer.

One hundred and fifty-nine patients with chronic ruptured ulcer were admitted to hospital during the period investigated. A few other ulcers were classed as acute and will not be considered here. Of the 159 patients, 102 had

Acute Erosion of the Stomach and Duodenum.

There were 74 cases of acute erosion of the stomach and duodenum. Forty-three of these patients were males and 31 females—a preponderance of males in the proportion 3:2. This is a much smaller excess of males than occurs in cases of either ruptured or chronic ulcer.

It is of interest that no acute erosions occurred in people aged under twenty years, and also that the average age of the females falls somewhat below that for the males (Table IV).

ADMISSIONS AND DEATH RATE.

Of the 1,027 cases reviewed, 82 were fatal; that is, the mortality rate was 8.0%. When these cases were considered in more detail it was found that 40 patients had chronic ulcers, 39 had ruptured ulcers, and three had acute erosions of the stomach or duodenum. There were 159 ruptured ulcers and 763 chronic ulcers, so it can be seen that the mortality rate for the former is very high; in fact, if death from ruptured ulcer could be prevented, the total mortality rate *per centum* would be only 4.1, approximately half the present figure.

DETAILED DISCUSSION OF GROUPS.

Each of the above-mentioned three groups of cases will now be dealt with in more detail.

TABLE II.

Number of Patients.	Males.				Females.			
	Age Groups. (Years.)				Age Groups. (Years.)			
	12-19	20-39	40-59	60 and Over.	12-19	20-39	40-59	60 and Over.
Chronic Gastric Ulcer (Ruptured Ulcer Excluded).								
Total in six years ..	1	32	118	62	—	5	23	14
Percentage	0.5	15.0	55.4	29.1	—	—	—	—
Ratio M. : F.	5.1 to 1.0							
Chronic Duodenal Ulcer (Ruptured Ulcer Excluded).								
Total in six years ..	8	142	208	84	—	20	30	16
Percentage	1.7	30.7	47.6	19.0	—	30.3	45.5	24.2
Ratio M. : F.	87.0% (6.7 to 1.0) 13.0%							

TABLE III.
Ruptured Ulcer.

Number of Patients.	Males.				Females.			
	Age Groups. (Years.)				Age Groups. (Years.)			
	12-19	20-39	40-59	60 and Over.	12-19	20-39	40-59	60 and Over.
Gastric.								
Total in six years ..	—	17	61	19	—	1	3	1
Ratio M.: F.	19.4 to 1.0							
Duodenal.								
Total in six years ..	1	21	25	8	—	—	2	—
Ratio M.: F.	27.6 to 1.0							

TABLE IV.
Acute Erosion.

Number of Patients.	Males.				Females.			
	Age Groups. (Years.)				Age Groups. (Years.)			
	12-19	20-39	40-59	60 and Over.	12-19	20-39	40-59	60 and Over.
Total in six years ..	—	12	23	8	—	12	14	5
Ratio M.: F. ..	1.4 to 1.0							

Chronic Peptic Ulcer.

There were 763 cases in this group and 40 of the patients died—a mortality rate of 5.3%. Of these 40 deaths, 23 (3.0%) were from gastric ulcer and 17 (2.3%) from duodenal ulcer.

The details of the causes of death are shown in Table V. Although the majority of patients had a duodenal ulcer, most of the deaths occurred in the gastric ulcer group. Thus gastric ulcer is a more fatal disease than duodenal ulcer. It will be noticed that hæmorrhage was the cause of death in most cases and that subphrenic abscess was fatal only in cases of gastric ulcer. An unexpected finding was that the deaths from post-operative shock all occurred after a gastro-enterostomy had been performed. The one patient who died from post-operative cardiac failure had suffered from a cardiac disorder before the operation.

TABLE V.
Causes of Death.

Cause of Death.	Gastric Ulcer. ¹	Duodenal Ulcer. ²
Hæmorrhage	13	8
Subphrenic abscess .. .	2	—
Post-operative:		
Peritonitis and ileus .. .	3	3
Shock	1	3
Pneumonia	3	1
Hæmorrhage	—	1
Subphrenic abscess .. .	1	—
Cardiac failure	—	1

¹ Gastric ulcer, 255 patients, 23 died (9.0% mortality rate).

² Duodenal ulcer, 508 patients, 17 died (3.3% mortality rate).

The post-operative deaths were further analysed as follows: (i) partial gastrectomy, four gastric ulcers and six duodenal ulcers; (ii) gastro-enterostomy, three gastric ulcers and three duodenal ulcers; (iii) simple excision, one gastric ulcer. It can be seen that the total post-operative deaths were nearly equally divided between gastric ulcer and duodenal ulcer. However, 50 patients with gastric ulcer were operated on (26 partial gastrectomies, 17 gastro-enterostomies and seven excisions), while only 34 patients with duodenal ulcer were subjected to operation (19 partial gastrectomies and 15 gastro-

enterostomies)—an excess of 3:2 in favour of gastric ulcer. So it is seen that the post-operative death rate is 50% higher for duodenal ulcer than for gastric ulcer. The average age at death was 61.7 years in cases of gastric ulcer and 53.7 years in cases of duodenal ulcer. This difference is not surprising when it is remembered that duodenal ulcer occurs more in the lower age groups.

No patients, male or female, died from gastric ulcer under the age of forty years, while among those aged over forty years the mortality rate among gastric ulcer patients is higher for females than for males (13.5%:10.0%). In cases of duodenal ulcer the mortality rate was much higher for males than for females (4.4%:2.2%). The preponderance of duodenal ulcer over gastric ulcer is quite clear from Table VI and is particularly noticeable in patients aged under forty years.

Ruptured Peptic Ulcer.

One hundred and fifty-nine patients suffering from ruptured ulcer were admitted to hospital during the period investigated, and 39 died as a direct result of the condition. This is a mortality rate of 24.5%, which is very high indeed. The details of the causes of death are shown in Table VII. It will be seen that peritonitis, with ileus, and pneumonia are the two chief causes of death in cases of ruptured ulcer. The average age at death was 58.3 years in cases of gastric ulcer, while in cases of duodenal ulcer it was 48.3 years. Between the onset of symptoms and operation the time lag varied; but the great majority of patients were operated upon less than nine hours after the pain was first felt.

Of the 159 ruptured ulcers, 57 were duodenal ulcers while 102 were gastric ulcers—a proportion of 2:1 in favour of gastric ulcer. Thus the total mortality rate of gastric ulcer is 14.5% and that for duodenal ulcer is 10.0%. The corrected mortality rate, as seen in Table VII, is 22.5% for gastric ulcer and 28.1% for duodenal ulcer. This shows that the percentage of deaths from ruptured duodenal ulcer was higher than that of deaths from ruptured gastric ulcer.

Over four times as many patients suffering from ruptured gastric ulcer were aged over forty years as under, but the number of patients suffering from ruptured duodenal ulcer and aged over forty years was only one and a half times as great as the number of patients aged under

TABLE VI.
Admissions to Hospital and Deaths from Chronic Peptic Ulcer in a Period of Six Years.

Type of Ulcer.	Total Admissions.	Under 40 Years.			Over 40 Years.			
		Admissions.	Deaths.	Mortality Rate. (Per Centum.)	Admissions.	Deaths.	Mortality Rate. (Per Centum.)	
Males.								
Gastric ulcer	233	33	—	—	180	18	10.0	
Duodenal ulcer	429	150	2	1.3	299	13	4.4	
Females.								
Gastric ulcer	42	5	—	—	37	5	—	
Duodenal ulcer	66	20	1	—	46	1	—	

forty years. This again emphasizes the fact that duodenal ulcer occurs earlier in life than does gastric ulcer (Table VIII). In both ruptured gastric ulcer and ruptured duodenal ulcer the mortality rate *per centum* is much higher among patients aged over forty years than among younger patients.

Acute Erosion of the Stomach and Duodenum.

There were 74 cases of acute erosion of the stomach and duodenum, and although male patients still predominated, there were relatively many more female patients than in

TABLE VII.
Ruptured Ulcer.

Cause of Death.	Gastric Ulcer. ¹	Duodenal Ulcer. ²
Peritonitis and ileus	17	10
Post-operative pneumonia	4	2
Post-operative hæmorrhage	1	1
Post-operative shock	1	2
Cardiac failure	—	1

¹ Gastric ulcer, 102 cases, 23 deaths (22.5% mortality rate).

² Duodenal ulcer, 57 cases, 16 deaths.

the chronic ulcer series (Table IX). More cases were found among patients aged over forty years than among younger subjects; but this preponderance is much less pronounced among females than among males.

The total mortality was three out of the 74 patients, and all died of hæmorrhage. The only deaths were among males aged over forty years, and their average age was 59.3 years.

COMMENT.

The incidence and death rate of chronic gastric ulcer and duodenal ulcer have been considered separately for comparison.

A number of investigators are quoted by Walton,⁽¹⁾ all of whom found that the incidence of duodenal ulcer exceeded that of gastric ulcer. In his own series, how-

TABLE VIII.

Admissions to Hospital and Deaths from Ruptured Ulcer in a Period of Six Years.

Type of Ulcer.	Total Admissions.	Under 40 Years.		Over 40 Years.	
		Admissions.	Deaths.	Admissions.	Deaths.
Males.					
Gastric ulcer ..	97	18	1	79	20
Duodenal ulcer	55	22	4	33	12
Females.					
Gastric ulcer ..	5	1	—	4	2
Duodenal ulcer	2	—	—	2	—

ever, Walton found 621 (56.2%) uncomplicated gastric ulcers, 428 (38.8%) duodenal ulcers, and 55 (5.0%) combined lesions. Nichol⁽²⁾ also reviews the literature, and his findings are that the incidence of duodenal ulcer exceeds that of gastric ulcer all over the world except in London, where the lesions occur in equal numbers. In my own investigation there were 357 (37.5%) gastric ulcers, 565 (59.3%) duodenal ulcers, 20 (2.1%) combined lesions, and 11 (1.1%) stomal ulcers. These figures approximately agree with those of many writers, but are almost the reverse of those given by Walton. All his cases were proven at operation, and more gastric ulcer subjects may have needed operative treatment. More recently, Tidy,⁽³⁾ in a review of cases at Saint Thomas's Hospital, found that in the last few years an appreciable excess of gastric ulcer over duodenal ulcer had occurred. Cleland,⁽⁴⁾ in a

discussion of post-mortem findings at the Royal Adelaide Hospital, supported Walton's figures. He found that gastric ulcer exceeded duodenal ulcer in the proportion of 3:2. As peptic ulcer patients are for the most part ambulatory, many of them do not come to autopsy, and so from the clinical point of view post-mortem figures for peptic ulcer are not reliable.

All writers are agreed that male patients predominate in cases of both gastric ulcer and duodenal ulcer, but few give such a high ratio as seven males to one female, as was found for both gastric ulcer and duodenal ulcer in my series.

In a review of 944 cases reported in Canada, Lynch⁽⁵⁾ found the maximum age incidence between twenty and forty years, and could find no difference between the incidence of gastric ulcer and that of duodenal ulcer. From my figures it is evident that duodenal ulcer is a disease which occurs in younger people than gastric ulcer, although the maximum incidence for both is between the ages of forty and sixty years. Seventy *per centum* of the patients with duodenal ulcer in this investigation were aged over forty years, but 85% of the patients with gastric ulcer exceeded this age.

TABLE IX.

Admissions to Hospital and Deaths from Acute Erosion of the Stomach and Duodenum.

Period.	Total Admissions.	Under 40 Years.		Over 40 Years.	
		Admissions.	Deaths.	Admissions.	Deaths.
Males.					
Total in six years	43	12	—	31	3
Females.					
Total in six years	31	12	—	19	—

Combined gastric ulcer and duodenal ulcer is mentioned by Walton as occurring in 5.0% of cases. This combination occurred in only 2.1% of the cases under discussion.

Tidy found in his series that the overall mortality rate was 10% and that most deaths occurred among patients aged over forty years. In this inquiry the mortality rate was 8.0% and the age incidence was also similar to that of Tidy's series. It was also found, when ruptured ulcers were excluded, that 9.0% of patients with gastric ulcer died, while only 3.3% of patients with duodenal ulcer did so. This indicates that gastric ulcer is a much more fatal disease than duodenal ulcer.

So far as I can discover, all except one previous investigator gave the incidence of ruptured duodenal ulcer as higher than that of ruptured gastric ulcer. For example, Gibson⁽⁶⁾ in 123 cases found 44.7% of gastric ulcer and 55.3% of duodenal ulcer, and Williams and Walsh⁽⁷⁾ in 158 cases found 25% of gastric ulcer and 75% of duodenal ulcer, while Tidy in 263 cases found that the incidence of gastric ulcer (55.0%) exceeded that of duodenal ulcer (45.0%). In my series of 159 ruptured ulcers, 102 (64.2%) were gastric ulcers and 57 (35.8%) duodenal ulcers, an advantage of almost 2:1 in favour of gastric ulcer. As there were many more cases of chronic duodenal ulcer than gastric ulcer, the latter has a much greater liability to perforation. This finding differs from Tidy's; he found that duodenal ulcer has a greater liability to perforation than gastric ulcer. This difference is hard to explain, but the higher incidence of perforated gastric ulcer is not unreasonable, since a gastric ulcer is free to rupture into the peritoneal cavity over a much greater area of stomach than is a duodenal ulcer in the duodenum.

In cases of ruptured ulcer the proportion of male to female patients is very high. Figures given by Gibson state the ratio to be 24 males to one female, and those given by Williams and Walsh state the ratio as 25 males

to one female. In this investigation of 159 cases, in gastric ulcer the ratio was 19.4 males to one female, while in duodenal ulcer the ratio was 27.6 males to one female.

The death rate in the ruptured ulcer cases in the present series was 24.5%; for gastric ulcer it was 22.5% and for duodenal ulcer 28.1%. Gibson gives his death rate at 18.7%, the individual figure for gastric ulcer being 16.3% and that for duodenal ulcer 20.5%, while Williams and Walsh record a mortality rate of 30.0%, giving 61.8% for gastric ulcer and 20.9% for duodenal ulcer. All these figures are very high; but the set last given is the only one in which the mortality rate is higher for gastric ulcer than for duodenal ulcer. So it can be seen, in the present series, that although gastric ulcer is more liable to perforation than is duodenal ulcer, patients suffering from duodenal ulcer are more likely to die from this cause.

TABLE X.
Admissions to Hospital, Gastric Ulcer and Duodenal Ulcer.

Month.	Gastric Ulcer.	Duodenal Ulcer.	Total.
January	15	36	51
February	19	42	61
March	21	50	71
April	10	49	59
May	35	45	80
June	28	53	81
July	25	50	75
August	20	48	68
September	20	46	66
October	23	33	56
November	18	31	49
December	21	25	46

As the operative mortality rate of ruptured ulcers is so high, it is interesting to note the promising results obtained by Bedford-Turner,⁶⁰ who used conservative treatment. He gave morphine, and glucose and saline solution by the intravenous drip method, and passed a stomach tube to remove the gastric contents. After this the stomach contents were aspirated through a Ryle's tube every half-hour for the first twenty-four hours, every hour for the second twenty-four hours, and every three hours for the subsequent day. Among the six men with ruptured duodenal ulcer reported in this series there were no deaths.

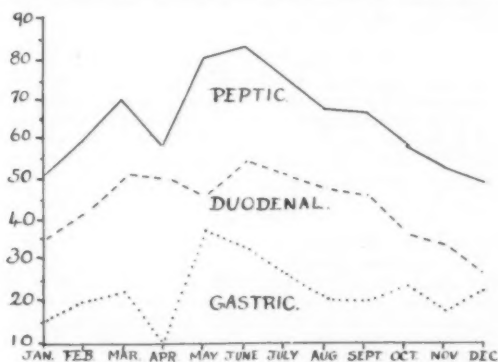


FIGURE I.

Walton reviews the work on acute erosion of the stomach and duodenum, and states that female patients exceed male patients by between two and four to one. In the 74 cases of acute erosion in the present series, male patients exceeded female patients by 1.4 to 1.

From the above discussion it can be noted that the incidence of peptic ulcer varies the world over, and it is found that gastric ulcer and duodenal ulcer differ (i) in their incidence, (ii) in the occurrence of duodenal ulcer in younger people than gastric ulcer, (iii) in the number of ulcers which rupture, and (iv) in their respective death rates.

MONTHLY INCIDENCE OF ADMISSIONS TO HOSPITAL.

In peptic ulcer cases a general rise in incidence was found from January to May and June and then a gradual falling off in numbers until December (Table X, Figure I). Thus attacks of severe peptic ulcer symptoms occur much less commonly in November, December and January than in the other months. This part of the year is the fresh fruit season in South Australia, and the extra supply of vitamin C may possibly account for the falling off in attacks. The figures for duodenal ulcer follow the same curve as the total figures for peptic ulcer, but those for

TABLE XI.
Position of Chronic Gastric Ulcer (134 Cases).

Position of Ulcer.	Number of Cases.	Percentage.
The cardia	2	1.5
The greater curvature	11	8.2
The upper part of the lesser curvature	18	13.4
The middle part of the lesser curvature	21	15.8
The lower part of the lesser curvature	31	23.1
Prepyloric site	51	38.0

gastric ulcer fall sharply in April, and this accounts for the variation in the total peptic ulcer curve. There is no apparent reason for this sudden drop in the incidence of gastric ulcer. Apart from this, May, June and July are the peak months for occurrence of gastric ulcer attacks, while during all the rest of the year, from August to April, a steady level is maintained. Thus, apart from the April drop, the rest of the curve for peptic ulcer is made by the incidence of duodenal ulcer.

POSITION OF CHRONIC GASTRIC ULCER.

The position of chronic gastric ulcer was determined for the three years 1939 to 1941 inclusive. There were 156 cases, but in 22 of these the position was not reported. This leaves 134 cases for our consideration. It was found that over 60% of gastric ulcers occurred in the pyloric

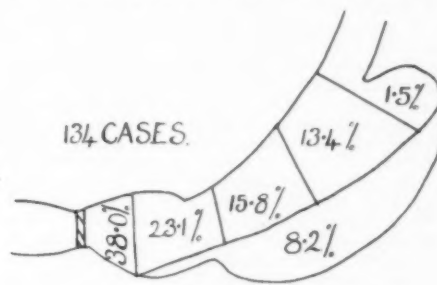


FIGURE II.

antrum and prepyloric regions of the stomach (Table XI, Figure II) and that the percentage became progressively smaller as the cardia was approached. In 8.2% of cases the ulcer was on the greater curvature of the stomach; this is a surprisingly high figure. In only two cases was more than one gastric ulcer present in the same patient; but in neither of these was the position of the ulcers reported.

SYMPTOMATOLOGY.

The symptoms of peptic ulcer were investigated in detail. Separate consideration was given to those of gastric ulcer and duodenal ulcer to determine if there were any differences which would enable the diagnosis of one or the other to be made clinically with some certainty.

Investigation of the symptoms in the cases of combined gastric ulcer and duodenal ulcer and in cases of stomal ulcer was also undertaken.

Consideration was given to the symptoms in the following order: pain (the position, the time of occurrence,

and whether relieved by food or powders); vomiting (occasional or frequent); hæmorrhage (hæmatemesis or melena); appetite (good, fair or poor) and whether the patient was afraid to eat; bowel condition (constipated, regularly open or loose); weight (gained, constant, or lost). In addition, inquiry was made into the reason for admission to hospital, and the time of occurrence of pain was compared with the position of the ulcer. The result of fractional test meals was also noted, as was the number of patients who drank alcoholic beverages or smoked tobacco.

The average age of chronic peptic ulcer patients was fifty-one years; that of gastric ulcer patients was fifty-four years and that of duodenal ulcer patients was forty-eight years. This emphasizes, as has previously been shown, the fact that duodenal ulcer occurs in younger people than gastric ulcer.

The duration of symptoms of both gastric ulcer and duodenal ulcer varied between two months and twenty-two years; but the average duration was five years.

Pain.

Position.

Well over 80% of both gastric ulcer and duodenal ulcer patients had epigastric pain, but of these, twice as many with duodenal ulcer as with gastric ulcer had pain elsewhere in addition. The majority of these pains associated with epigastric pain were felt in the back, but some were situated in the right iliac fossa, in the chest, in the left shoulder, in both shoulders, in the hypogastrium, in the left iliac fossa, and in the left groin. In a smaller percentage of cases pain also occurred predominantly in the following situations: the right hypochondrium, the left hypochondrium, the hypogastrium, the left iliac fossa, the right iliac fossa, the right loin, and the chest. An appreciable number of patients with gastric ulcer and duodenal ulcer had no pain at all, this state of affairs being most prevalent among the duodenal ulcer patients.

From the figures mentioned above the following conclusions were drawn: (i) Pain which occurred in the left shoulder or in both shoulders in association with epigastric pain was found only in cases of duodenal ulcer, but there are no positions where pain occurred which belong exclusively to gastric ulcer. (ii) Four times as many gastric ulcer patients as duodenal ulcer patients had chest pain in association with epigastric pain. The patient who had chest pain only was suffering from a gastric ulcer. (iii) In general there were more duodenal ulcer patients than gastric ulcer patients who had pain in the right hypochondrium and right iliac fossa, and fewer who had pain in the left hypochondrium and the left iliac fossa and *vice versa*. That is, duodenal ulcer pain tends to the right side and gastric ulcer pain to the left. (iv) Three times as many duodenal ulcer patients as gastric ulcer patients had pain only in the hypogastrium. (v) Many more duodenal ulcer patients than gastric ulcer patients had no pain at all (7.0% of duodenal ulcer patients and 4.7% of gastric ulcer patients). Those patients who had no pain at all complained chiefly of hæmatemesis, melena, vomiting and loss of weight, as shown in Table XII. In these cases hæmatemesis is more common in duodenal ulcer than in gastric ulcer, while melena, vomiting and loss of weight predominate in gastric ulcer.

Time Relation of Pain to Food et cetera.

It was found that the majority of both gastric ulcer and duodenal ulcer patients had pain one hour or less after food (Table XIII). However, considerably more gastric ulcer than duodenal ulcer patients came in this group. As would be expected, the percentage of duodenal ulcer exceeds that of gastric ulcer in groups in which pain was felt two hours and less after food, in three hours and less after food, and in more than three hours after food; but this excess is not nearly so pronounced as is often stated. The proportions of gastric ulcer and duodenal ulcer patients with pain having no relation to food and with continuous pain are about the same. Pain occurred at night as well as in the daytime three times as commonly in duodenal ulcer as in gastric ulcer.

TABLE XII.
Patients with No Pain (48 Cases).

Symptoms.	Gastric Ulcer. (12 Patients.)	Duodenal Ulcer. (36 Patients.)
Hæmatemesis	5	26
Melena	3	4
Vomiting	3	5
Loss of weight	1	1

Thus it is clear that no reliable indication of the position of the ulcer can be gained by the time relation of pain to food. However, the longer after food pain occurs, the more likely is it that a duodenal ulcer is present, and if pain occurs at night, then the odds are three to one in favour of this condition.

The fact that the time relation of pain to food is no reliable indication of the position of the ulcer is emphasized by the following figures taken from the cases studied. In gastric ulcer the position of the ulcer corresponded with the time after food of the occurrence of pain in only 36.6% of cases, while in duodenal ulcer agreement was found in only 21.8%. In the interpretation of these figures a liberal margin was allowed, one hour after food being taken as down to one-half to three-quarters of the way to the pylorus, two hours after food as half-way down to the pylorus, and three hours after food as from the pyloric antrum into the duodenum.

Relief of Pain by Food and Powders.

Food and powders were both found to relieve pain more in duodenal ulcer than in gastric ulcer (Table XIV). When food relieved pain, powders nearly always did so too; but the reverse was not true. Food relieved pain in surprisingly few cases, but the majority of patients were relieved by powders or food or by both.

Vomiting.

The number of patients who vomited was between 40% and 50% in both gastric ulcer and duodenal ulcer; but more gastric ulcer patients than duodenal ulcer patients vomited often. In this investigation, for a patient to be classified as vomiting often, he must have done so at least once a day (Table XV).

TABLE XIII.
Time Relation of Pain to Food (After Intake).

One Hour and Less.	Two Hours and Less.	Three Hours and Less.	More than Three Hours.	No Relation.	Pain Continuous.	Pain at Night.
Gastric Ulcer. (275 Cases.)						
60.9%	11.9%	7.0%	2.5%	12.3%	5.4%	9.0%
Duodenal Ulcer. (495 Cases.)						
40.0%	18.2%	14.4%	7.4%	13.7%	6.3%	27.5%

Hæmorrhage.

For the purpose of this inquiry it was considered that if a person had hæmatemesis he must also have had melena, so where melena is mentioned it has occurred without hæmatemesis. Three-fourths of patients with melena had a gross hæmorrhage, and the faces of one-fourth yielded a positive result to the test for occult blood.

Hæmorrhage occurs in a similar percentage of cases in gastric ulcer and duodenal ulcer, but the incidence of hæmatemesis is slightly higher in gastric ulcer. The percentage of patients with hæmorrhage was 40 to 45; this figure was somewhat lower than had been anticipated (Table XVI).

TABLE XIV.
Relief of Pain by Food and Powders.

Agent of Relief of Pain.	Gastric Ulcer. (275 Cases.)	Duodenal Ulcer. (495 Cases.)
Food	43.2%	64.5%
Powders, but not food .. .	59.6%	77.9%
Powders, food, or both .. .	72.7%	89.9%

Appetite.

Fewer duodenal ulcer patients than gastric ulcer patients had poor appetites, while more duodenal ulcer patients had good appetites. A most significant finding was that over three times as many gastric ulcer patients as duodenal ulcer patients were afraid to eat because of the early onset of discomfort and pain (Table XVII).

Condition of Bowels.

In this investigation constipation was considered present when the patient had to take aperients regularly. A high percentage of patients (44% to 55%) were found to be constipated, but more gastric ulcer than duodenal ulcer patients were troubled in this way and fewer had regular bowel actions (Table XVIII). It was noticed during the search through the case notes that in both gastric ulcer and duodenal ulcer constipation often dated from the commencement of the last attack, and this was particularly evident when the outstanding symptom was hæmorrhage.

TABLE XV.
Occurrence of Vomiting.

Degree of Severity.	Gastric Ulcer. (275 Cases.)	Duodenal Ulcer. (495 Cases.)
Vomiting occurred .. .	47.4%	42.9%
Vomiting frequent .. .	67.0%	58.2%
Vomiting occasional .. .	33.0%	41.8%

Weight.

A surprisingly high number of patients said that they had lost weight. Most of them had lost one or two stone in the preceding three to six months. Many more gastric ulcer than duodenal ulcer patients lost weight, while the weight of more of the latter remained constant or increased (Table XIX). The higher loss of weight in gastric ulcer may be due in part to the proportion of patients who fear to eat, and to the slightly more frequent vomiting, although loss of weight on the symptom charts was not exclusively associated with either of these factors.

From these figures it will be seen that loss of weight was a common symptom in both gastric ulcer and duodenal ulcer.

Reason for Admission to Hospital.

The chief complaint of 43% of both gastric and duodenal ulcer patients was that their pain had become worse. Associated with this, vomiting was found in 17% and 14% respectively of cases of gastric ulcer and duodenal ulcer,

while 23% of duodenal ulcer patients and only 4.6% of gastric ulcer patients had pain at night.

The next most common complaint was hæmatemesis, and similar percentages were found in gastric ulcer and duodenal ulcer.

Third in importance was vomiting, and fourthly, the patient complained that his previously intermittent pain had now become continuous. This last-mentioned condition is commonly associated with vomiting in both gastric ulcer and duodenal ulcer and with pain at night in gastric ulcer.

Melena was fifth on the list and was particularly prone to be the predominant symptom in duodenal ulcer. Loss of weight came next and was often found to occur in gastric ulcer.

TABLE XVI.
Occurrence of Hæmorrhage.

Type.	Gastric Ulcer. (275 Cases.)	Duodenal Ulcer. (495 Cases.)
Hæmorrhage .. .	44.4%	42.9%
Hæmatemesis .. .	62.9%	56.8%
Melena .. .	37.1%	43.2%

Attacks of pain became more frequent in only a few cases. However, it was often stated that attacks were becoming more frequent; but then the patient had hæmatemesis or some other complication.

Angina pectoris and constipation are the two remaining rare causes of admission to hospital in peptic ulcer, and they are particularly interesting. The angina occurred in a patient who had recently had severe hæmatemesis. In view of the severity of the hæmorrhages in some of the other cases, it is surprising that this does not occur more often. The man, who was admitted to hospital with severe constipation, was thought to be suffering from acute intestinal obstruction; but the only abnormality revealed by a searching investigation was a duodenal ulcer.

Summary of Symptoms.

1. Pain which is situated in the left shoulder or in both shoulders in association with epigastric pain occurs only in cases of duodenal ulcer.

2. Equal percentages of patients had epigastric pain; but twice as many duodenal ulcer as gastric ulcer patients had pain elsewhere as well.

3. Four times as many gastric ulcer as duodenal ulcer patients had chest pain in association with epigastric pain.

TABLE XVII.
Appetite.

Type.	Gastric Ulcer. (275 Cases.)	Duodenal Ulcer. (495 Cases.)
Poor .. .	44.8%	38.5%
Fair .. .	12.6%	13.6%
Good .. .	42.6%	47.9%
Patient afraid to eat .. .	22.4%	7.1%

4. The pain of duodenal ulcer tends to occur on the right side of the abdomen and that of gastric ulcer on the left.

5. Three times as many duodenal ulcer as gastric ulcer patients had pain only in the hypogastrium.

6. Many more duodenal ulcer than gastric ulcer patients had no pain at all.

7. The majority of gastric ulcer and duodenal ulcer patients have pain one hour or less after food, irrespective of the position of the ulcer.

8. Pain occurring at night was three times as common in duodenal ulcer as in gastric ulcer.

9. It has been clearly shown that the time relation of pain to food is not a reliable indication of the position of the ulcer.

10. Food relieved pain in more cases of duodenal ulcer than of gastric ulcer, and powders also relieved pain when food did not in more cases of duodenal ulcer than of gastric ulcer. Powders or food, or both, relieved pain in 70% to 80% of cases.

TABLE XVIII.
Condition of Bowels.

Condition.	Gastric Ulcer. (275 Cases.)	Duodenal Ulcer. (495 Cases.)
Constipated	55.5%	44.1%
Regular	42.3%	52.6%
Loose	2.2%	3.3%

11. A few less duodenal ulcer than gastric ulcer patients vomited at all; but of these many more gastric ulcer patients vomited at least once a day.

12. Hæmorrhage occurred in equal percentages of gastric ulcer and duodenal ulcer cases; but slightly more hæmatemesis and slightly less melenæ occurred in gastric ulcer than in duodenal ulcer.

13. Slightly more duodenal ulcer than gastric ulcer patients had good appetites and slightly fewer had poor appetites; but three times as many gastric ulcer as duodenal ulcer patients were afraid to eat.

14. More gastric ulcer than duodenal ulcer patients were constipated, and fewer had regular bowel actions.

15. Many more gastric ulcer than duodenal ulcer patients lost weight; but a high percentage of both did so.

TEST MEAL EXAMINATION.

Most of the fractional test meals were of gruel, but some were of alcohol. However, Bennett and Ryle's figures for the range of normal were used as a standard in both instances.

Test meal examinations were not made in all cases, but the figures were available in 482, which is an appreciable number. It was found (Table XX) that considerably more patients with duodenal ulcer had hyperchlorhydria, and fewer had normal gastric acidity, hypochlorhydria and achlorhydria than patients with gastric ulcer. The most outstanding feature was the number of cases of hypochlorhydria and achlorhydria occurring in both gastric ulcer and duodenal ulcer. This is especially surprising in the latter condition, as the percentage of patients with subnormal gastric acidity was 18.4.

TABLE XIX.
Patient's Weight.

Condition of Weight.	Gastric Ulcer. (275 Cases.)	Duodenal Ulcer. (495 Cases.)
Gained	3.8%	9.8%
Constant	22.1%	30.0%
Lost	74.1%	60.2%

TOBACCO AND ALCOHOL.

During this investigation a record was made of the patients who smoked tobacco and drank alcohol. Most smokers averaged two ounces of tobacco a week or its equivalent in cigarettes. Very little difference was found between the numbers of gastric ulcer and duodenal ulcer patients who smoked and drank (Table XXI). In each case about 80% smoked tobacco and 50% drank alcohol. This latter figure would appear to rule out alcoholic beverages as a major ætiological factor, while the former needs further investigation, as the number of smokers in the community is large.

COMBINED GASTRIC AND DUODENAL ULCERS.

There were only 20 patients with the combined lesions among 801 patients with chronic ulcer—an incidence of 2.5%. The average age was fifty-three years, which is in agreement with the figure for gastric ulcer. The sex ratio was 2.3 to 1.0 in favour of males, and this is much lower than for gastric ulcer or duodenal ulcer.

Symptoms and Signs.

The same detailed investigations were carried out for the combined lesions as for gastric ulcer and duodenal ulcer separately. However, only a condensed summary of the findings will be presented here.

TABLE XX.
Result of Test Meal Examination.

Gastric Acidity.	Gastric Ulcer. (162 Cases.)	Duodenal Ulcer. (320 Cases.)
Hyperchlorhydria	40.8%	62.2%
Normal	34.0%	19.4%
Hypochlorhydria	17.8%	12.5%
Achlorhydria	7.4%	5.9%

1. The combined lesions did not occur in cases in which the history was short; they occurred only in old-established cases. For the most part the ulcers occurred on either side of the pylorus, often joining through the canal. In only one case was there a duodenal ulcer with a gastric ulcer high on the lesser curvature of the stomach.

2. All patients had pain and most had severe epigastric pain which was commonly continuous.

3. Nearly three-fourths vomited, and most did so frequently.

4. Forty per centum of patients had hæmorrhage, and one-half of these had it in the form of hæmatemesis. This is a similar percentage to that found in cases of gastric ulcer and duodenal ulcer occurring separately.

5. Well over one-half of the patients had a poor appetite and 17% were afraid to eat.

TABLE XXI.
Tobacco Smoking and Alcohol Consumption.

Use of Tobacco or Alcohol.	Absent or Present.	Gastric Ulcer. (61 Cases.)	Duodenal Ulcer (274 Cases.)
Tobacco smoking ..	Present. Absent.	82.0% 18.0%	78.1% 21.9%
Alcohol consumption ..	Present. Absent.	56.7% 43.3%	51.0% 49.0%

6. One-fifth of the patients had loose bowel actions (a rather large proportion).

7. Ninety per centum of patients had lost weight.

8. Two-thirds had a high gastric acidity curve.

The above list details the main points distinguishing the combined lesions. Although there were no symptoms which occurred only in the presence of this condition, there were a number of outstanding points, and these have been noted above.

STOMAL ULCERS.

Eleven stomal ulcers occurred in 801 cases of chronic ulcer—an incidence of 1.4%.

Of all the gastric ulcer patients investigated, 3.1% had previously undergone gastro-enterostomy, and of the duodenal ulcer patients 3.4% had undergone this operation. It was also found that during the six years of this investigation 30.6% of the chronic peptic ulcer patients who had undergone a previous gastro-enterostomy were admitted to hospital and diagnosed as suffering from stomal ulcer.

The average age of stomal ulcer patients was fifty-five years, which is much the same as that for gastric ulcer patients.

A long history of peptic ulcer was found in all cases of stomal ulcer.

Although a detailed chart of symptoms was prepared, only a brief description of the main findings will be submitted here.

Symptomatology.

Pain.

The percentage of patients with epigastric pain was somewhat lower than in gastric ulcer and duodenal ulcer, but the percentage of those with no pain was very high indeed (27.0). All of the latter had severe melena. Of the patients who had pain, none had any more than two hours after food and 50% had pain at night (a very large proportion).

A rather surprising finding was that food relieved pain in 80% of cases, while the remaining patients were all relieved by powders.

Vomiting.

A relatively low percentage (36) of patients vomited, but three-quarters of these vomited often.

Hæmorrhage.

The outstanding feature with regard to hæmorrhage was the finding that over 90% of patients had hæmorrhage and that 60% of these had melena.

Appetite.

The proportion of patients with poor appetite was the same as in gastric ulcer, but a larger number of patients with fair appetite and less with good appetite were found than in either gastric ulcer or duodenal ulcer.

Condition of Bowels.

The percentages of cases of constipation and of regular bowel actions were as for gastric ulcer—that is, 55% and 45% respectively.

Weight.

Comparatively few patients (44%) lost weight. In gastric ulcer and duodenal ulcer 60% to 70% did so.

Test Meals.

Only two patients had test meal examinations, and the results of both these were normal. This is both surprising and interesting; but no conclusions can be drawn from two cases.

Summary of Characteristics of Stomal Ulcer.

Thus, summarized, the characteristics of stomal ulcer are (i) a history of a previous gastro-enterostomy, (ii) the occurrence of pain two hours or less after food, and at night, which is always relieved by food or powders, or both; in addition possibly melena or hæmatemesis may occur; (iii) melena with no pain.

DISCUSSION.

The majority of the articles on peptic ulcer in the literature of the last thirty years are concerned with the aetiology and surgical treatment of the condition. A few discuss the incidence; but few review the symptomatology of the disease. This may be because such a detailed investigation is tedious and few have had the time to undertake it. An enforced rest enabled me to undertake the present investigation.

On the subject of peptic ulcer, Walton⁽¹⁾ has stated that "if the history is typical the diagnosis is as certain and clearly defined as any known surgical lesion, but if it be in any way atypical the case is almost certain not to be one of ulcer". This statement does not hold for ulcers in South Australia, as it can be seen from this report that there is great variation in the symptoms of which a patient may complain. In his investigation Walton found that the typical gastric ulcer history was one in which epigastric pain occurred, often radiating to the back. This

pain had a pronounced periodicity, with complete freedom between attacks. In duodenal ulcer he found that the pain occurred rather more to the right than that of gastric ulcer and that it had considerably less tendency to radiate. This pain had the same periodicity as that of gastric ulcer and was found occasionally to pass to the right iliac fossa. When mentioning gastric ulcer, Walton makes the following statement:

Careful investigation of clinical history controlled by operative findings has shown that the time of onset of pain is of very great value in determining the site of the ulcer. If it be situated high up on the lesser curve the pain will appear shortly after food, while if placed near the pylorus it may come on late and may even wake the patient in the night, thus suggesting a duodenal ulcer.

While discussing duodenal ulcer, Walton states that the onset of pain has a definite relationship to the taking of food. It occurs late after food, so that the patient may note that it appears before the next meal, or he may say that it commences two or three hours after the meal is taken. It is constantly found that the patient is awakened at night by pain commencing usually about one or two o'clock in the morning. Pain is relieved by the taking of food, while in gastric ulcer this is not so common.

Many of the above-mentioned features of ulcer pain coincide with the findings in my series; but there are some features which do not occur in cases of peptic ulcer in South Australia, and these will now be discussed.

The periodicity of attacks of pain with complete freedom in between was an outstanding feature of 72% of cases of gastric ulcer and 69% of cases of duodenal ulcer in this survey. This is not nearly so common as Walton states it to have been in his cases. The remaining 30% or so of patients were divided as follows: 18.4% of gastric ulcer patients and 17.3% of duodenal ulcer patients were in the throes of their first attack, which had continued uninterruptedly for from two to six months; 9.0% of gastric ulcer patients and 10.8% of duodenal ulcer patients had had one previous attack a year or more before their admission to hospital and had been free from symptoms until the present attack began a few days or weeks before; while 0.8% of gastric ulcer patients and 0.4% of duodenal ulcer patients were afflicted with repeated attacks of vomiting at intervals, but had no pain at all. The remaining 3.0% of duodenal ulcer patients had repeated hæmatemesis with no associated pain, and this condition occurred only in duodenal ulcer. So it can be seen that variation from Walton's typical picture is not uncommon here, and the cases which do vary fall into the four groups mentioned above.

In his series Walton stated that duodenal ulcer pain rarely radiated while gastric ulcer pain often did so, whereas I found, as stated above, that twice as many duodenal ulcer patients as gastric ulcer patients had pain elsewhere besides the epigastrium. The relationship of pain to food was not so pronounced in Walton's review, and there was no definite relationship between the position of the ulcer and the time relation of pain to food, as he states. In fact, in only 36.6% of cases of gastric ulcer and 21.8% of cases of duodenal ulcer was there any such association between the position of the ulcer as seen on fluoroscopic examination and the time after food at which the pain occurred. Night pain was not nearly so common in this series as in Walton's, although it was three times as common in duodenal ulcer as in gastric ulcer.

Walton's figures for the remaining symptoms were as follows: (i) vomiting was present in 88% of cases of gastric ulcer and in only about 30% of cases of duodenal ulcer, and in most of the latter vomiting was not severe; (ii) hæmorrhage (this includes only gross hæmorrhage) occurred in 29% of cases of gastric ulcer and in 23% of cases of duodenal ulcer; (iii) the appetite was good in nearly all cases of gastric ulcer and duodenal ulcer, but most gastric ulcer patients are afraid to eat; (iv) with regard to weight, both gastric ulcer and duodenal ulcer patients are typically plump, although slight loss of weight may occur in an acute attack; (v) constipation is not

uncommon in cases of duodenal ulcer, but some gastric ulcer patients have a tendency to diarrhoea.

Much less vomiting occurred in the South Australian cases, and the preponderance of vomiting in gastric ulcer was much less marked. The patients who vomited were 47% of those suffering from gastric ulcer and 43% of those suffering from duodenal ulcer. Haemorrhage in the South Australian series was much more prevalent, even when about one-quarter is subtracted for positive results to tests for occult blood. Although duodenal ulcer patients with good appetite predominate in this series, they do not do so by much, while in gastric ulcer more patients had poor appetite than good. The figures show that three times as many gastric ulcer patients as duodenal ulcer patients were afraid to eat; but the percentage of gastric ulcer patients is only 22, which is very few compared with those of Walton. In South Australia pronounced loss of weight is an outstanding symptom of peptic ulcer; it occurs in 74% of cases of gastric ulcer and in 60% of cases of duodenal ulcer, whereas Walton considers it of little importance. Contrary to the statements of the latter, the bowels of gastric ulcer patients in my series were more often constipated than those of duodenal ulcer patients (53% and 44% respectively), and the proportion is high in both.

The results of test meal examinations in Walton's series showed that 76% of gastric ulcer patients had hyperchlorhydria, 17% had normal gastric acidity, and 7% had hypochlorhydria, while in cases of duodenal ulcer the corresponding figures were 91%, 5.5% and 3.5%. The South Australian figures do not agree with Walton's; they revealed a smaller incidence of hyperchlorhydria and a higher incidence of hypochlorhydria and achlorhydria. So much was this so that in any one case the result of the fractional test meal examination could not be taken as in any way aiding the diagnosis. Lynch⁽⁵⁾ gives figures for the results of fractional test meals in 944 cases in Canada which agree much more nearly with those found in South Australia.

Walton found that in 5% of his 1,104 cases gastric ulcer and duodenal ulcer occurred together in the one patient, and he quotes other authors with figures ranging from 3.2% to 14.0%. In the present investigation 20 cases occurred. This is an incidence of 2.5%, which is rather lower than any quoted above.

Hurst and Stewart⁽⁶⁾ state that the symptoms of gastro-jejunal ulcer are similar to those of duodenal ulcer, but that the time of onset of pain is less regular and is less completely relieved by food and powders. They state that vomiting is rare and that haematemesis and melena may occur with no previous symptoms. With the latter two statements my findings agree; but in this series pain most often occurred regularly within two hours after a meal, and although 50% of patients had pain at night, all without exception had their pain relieved by food or powders or both. Walton states that among surgeons of wide experience there is remarkable unanimity in placing the frequency of gastro-jejunal ulcer between 1% and 2%. Figures are difficult to determine, but in South Australia they must be much higher than this, as 30.6% of patients with a chronic peptic ulcer, who had undergone a previous gastro-enterostomy, were found to have a stomal ulcer during the six years of this investigation.

SUMMARY AND CONCLUSIONS.

The three main objects of this investigation were as follows: (i) to review the incidence, death rate and symptomatology of peptic ulcer in South Australia and to see if and where these differ from the findings in other localities; (ii) in all the findings under the first heading, to differentiate between gastric ulcer and duodenal ulcer and to discover any grounds for their separate aetiology and diagnosis; (iii) to inquire into the incidence and symptomatology of the combined ulcers and of stomal ulcer.

It has been shown that the incidence, death rate and symptomatology of peptic ulcer vary the world over. These three factors differ between gastric ulcer and duodenal ulcer and between males and females. Duodenal ulcer

was found to occur in younger people than gastric ulcer, while the proportion of males to females in both gastric ulcer and duodenal ulcer was seven to one. This figure is high, but not nearly so astonishing as the proportions for ruptured gastric ulcer (19 to 1) and for ruptured duodenal ulcer (28 to 1). The question why male patients exceed female patients in cases of chronic peptic ulcer, and especially in cases of ruptured ulcer, is fundamental and has not yet been answered. It is intimately bound up with the cause of the condition, which is also unsolved at the present moment.

A number of investigators have shown that the incidence of gastric ulcer and duodenal ulcer varies considerably, and use this fact as an argument in favour of a separate aetiology for each condition. The figures here support this different incidence; but I am not sure that it is sound to maintain that because of this there must be a fundamentally different cause—in other words, that they are two separate diseases. If this same argument was used, peptic ulcer, and especially ruptured ulcer, would be a different disease in men and women. It is difficult to see why two conditions with such similar symptoms could have different causes. Experimentally both gastric ulcer and duodenal ulcer have been produced under the same conditions, so it would be more logical to assume a common primary aetiological factor. The variation in incidence and rupture rate may be due to a combination of varying anatomical and physiological factors, with differing external and predisposing causes.

Sometimes it is held that one of these predisposing causes is the continued consumption of alcoholic liquor; but in this survey only 50% of ulcer sufferers drank alcohol at all. This would appear to rule this factor out as a major consideration in the aetiology of peptic ulcer, although it is undeniably the cause of some recurrences of symptoms. Tobacco smoking is another habit which has been blamed for the production of peptic ulcers. Of the peptic ulcer patients, 80% smoked; but most men in the community do so also. This must of necessity cancel the position of tobacco smoking as a primary factor in the aetiology, as 20% of patients were non-smokers. However, tobacco is undoubtedly an added irritant and its continued use predisposes the subject to a considerable number of recurrences.

Another outstanding finding is that ruptured gastric ulcer is twice as common as ruptured duodenal ulcer in South Australia, while the reverse is the case elsewhere. I can offer no explanation of this fact.

It is to be hoped, in view of these findings and of the importance of the disease to the general public, that similar inquiries will be undertaken in large centres of population elsewhere, so that an accumulation of evidence may eventually solve the riddle of peptic ulcer.

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REFERENCES.

- ⁽¹⁾ A. J. Walton: "The Surgical Dyspepsias", Second Edition, 1930.
- ⁽²⁾ B. M. Nichol: "The Geographical Distribution of Gastric and Duodenal Ulcers in the British Isles", *British Medical Journal*, November 29, 1941, page 780.
- ⁽³⁾ H. Tidy: "The Incidence of Peptic Ulcer at St. Thomas's Hospital, 1910-1937", *British Medical Journal*, March 10, 1945, page 319.
- ⁽⁴⁾ J. E. Cleland: "Gastric and Duodenal Ulcers in South Australia", *THE MEDICAL JOURNAL OF AUSTRALIA*, September 26, 1942, page 295.
- ⁽⁵⁾ E. Lynch: "An Analysis of Ulcer of the Stomach and Duodenum Based on a Study of 944 Case Reports", *The Canadian Medical Association Journal*, Volume XVII, 1927, page 677.
- ⁽⁶⁾ C. L. Gibson: "Acute Perforations of Stomach and Duodenum", *The Journal of the American Medical Association*, October 6, 1928, page 1006.
- ⁽⁷⁾ H. Williams and C. H. Walsh: "The Treatment of Perforated Peptic Ulcer", *The Lancet*, January 4, 1930, page 9.
- ⁽⁸⁾ E. W. Bedford-Turner: "Conservative Treatment of Duodenal Ulcer", *British Medical Journal*, March 31, 1945, page 457.
- ⁽⁹⁾ A. F. Hurst and M. J. Stewart: "Jejunal and Gastro-Jejunal Ulcers", *The Lancet*, October 13 and 20, 1928, pages 742 and 805.

SURGERY IN TWO WORLD WARS.¹

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"SURGERY is based on unchanging principles, not on fads of the moment." This remark of Brigadier W. A. Hailes remains true in spite of the efforts of the young and enthusiastic to suggest new technical instructions, each more volatile than the last, and in spite of pitying remarks by those full of strife and new ideas when they are referred to principles recorded years ago.

By 1918 the principles of war surgery were firmly established, and, being principles, they stand unchanged today. These are the principles:

1. Primary operation should be carried out before the onset of invasive infection. This period is roughly six to eight hours from the time of receipt of the wound—the golden period.
2. Primary operation should be as completely as possible an excision of fouled and devitalized tissue and removal of foreign material.
3. Efficient drainage should be provided and the wounds left unsutured. Exceptions to this are wounds penetrating the head, chest, abdomen and large joints.
4. Rest for injured structures is important.
5. Early transportation of the severely wounded is dangerous.
6. Accessory to the preceding principles great importance is laid upon (a) early collection of wounded; (b) minimum interference on the journey to the surgical station; (c) careful sorting—"triage", as the French call it—with segregation into groups, such as "immediate", "X-ray", "resuscitate", "moribund"; (d) resuscitation; (e) essential preventive measures with tetanus toxoid, antitetanus serum, "Atebrin" *et cetera*.

In the later stages the struggle resolves itself into (i) the fight against sepsis, (ii) restoration of bodily health, (iii) restoration of function.

These principles seem to us now so self-evident that it is hard to believe how ignorant we were in 1914. Previous wars were of little help; they had been largely struggles against disease, struggles to maintain sufficient men in the field. Their surgery was truly the surgery of sepsis. Industry and traffic were only beginning to pile up their quota of trauma. Moreover, 1914 brought in new weapons—higher explosive, greater fragmentation—and, particularly in Flanders and France, greater fouling of wounds. Very early it was realized that wounds caused by projectiles of high or medium velocity, carrying in foul clothing and dirt, were different from the wounds of industry and traffic.

In the original British Expeditionary Force the surgical set-up was that urgent surgical treatment should be done in the field ambulance. This resolved itself into the arrest of hæmorrhage, the amputation of a mangled limb, and superficial cleansing of wounds, application of splints *et cetera*, in conformity with Boer War practice. All other surgical treatment was to be carried out at the base. Two casualty clearing stations were nebulous; abdomens were not operated upon.

The field ambulance equipment was good, even if the personnel was not highly qualified or practised in surgery. The "regulars" were well steeped in sick parade tactics and in the lore of general administration; but any professional keenness had of course led to seconding to special jobs or hospital units. About one-third of the officers in the actual field were temporary or special reserve men. Even the men who were then the youngsters of the house surgeon type or very junior practitioners enjoyed a spurious reputation, for the soldier of the day had a deep-rooted suspicion and distrust of the Royal Army Medical Corps. In the Boer War the Government had tried the

scheme of "civil surgeons"—civilian medical men attached to the forces without commissioned rank. Naturally the soldier quickly assessed their lack of authority and used to tell them in no uncertain terms what they could do with their medicine. So for 1914 the surgeons were all commissioned. But the idea still lived.

It was not until after Mons, when the army was balked on the Aisne and the cavalry had fallen back in support, that an operating theatre was really established in the little town of Braisne. Very soon that was replaced by a stationary hospital, but some of the medical and surgical staff continued to work with its personnel and saw for the first time the sequence of events in neglected battle wounds. In this first period of trench fighting many of the wounded had been lying out for two, three or even four days, and sepsis was well advanced. Soldiers with compound fractures, inadequately splinted, lay in agony. Gas gangrene was rife. Amputations were frequent. Frankly, everyone seemed to be nonplussed. The fortunate victims localized their sepsis and later had their abscesses opened. Others fell victims to septicæmia. In many cases incisions intended to help drainage seemed to precipitate the onset of septicæmia. News then came that such casualties as had been able to be moved during the earlier period had arrived at the base in a terrible condition and that the mortality rate was high.

Early it became evident to the surgeons at the base that drainage was the important point. Men with wide open though extensive wounds did better than those with a smaller entrance wound and severe damage inside. This was the era of septic surgery and the birth of *débridement*. *Débridement* means cleansing and incision to provide drainage. The brawny, indurated surroundings of infected wounds were dangerous to incise; too often such interference was followed by streptococcal septicæmia and a long and frequently fatal illness. In September, 1914, the incidence of tetanus reached its highest at 0.88% of all wounded. The use of antitetanus serum commenced early in 1915.

At the base the younger surgeons, largely men of the registrar and junior surgeon class, were having continual disagreements with the administration. The young men could see that surgery held out the best chance, and it appeared that the earlier the surgical intervention, the better. The French are credited with the introduction of excision; but it would appear that it was an evolution rather than an introduction, and occurred naturally to many workers at the same time. The basic idea was to excise the wound *en bloc*, leaving practically an aseptic cavity. This is possible in only a few cases, and excision came to mean the removal of all accessible fouled and devitalized tissue *plus* foreign material. With the introduction of the idea of early excision, primary surgical treatment migrated from the base to the forward area, and the casualty clearing station as we know it was born.

In the years between the wars, although the basic principles of war surgery did not change, some powerful weapons were added to the surgeon's armament. Chief among these were (i) the discovery and development of the sulphonamides, (ii) the introduction and development of drip methods of transfusion, blood storage and the use of serum. Other innovations of importance are (i) improved plaster technique and Winnett-Orr methods, (ii) improved fracture technique, (iii) continuous stomach suction, (iv) the use of tetanus toxoid.

Of great importance in the later stages of treatment are (i) the improvements and developments in plastic surgery, (ii) the study of the chemistry of convalescence (blood, serum *et cetera*), (iii) the study of amputations and prostheses, (iv) the art of reconditioning.

This recent war started with all the advantages of experience gained in the last war and in the greatly increased number of traumatic cases which had been handled in the interval. The equipment was good, with a few weak spots here and there, most of which were triumphantly abolished.

It was evident from the campaigns in Europe that the tempo of this encounter was to be vastly different from

¹ Read at a meeting of the Victorian Branch of the British Medical Association on July 3, 1946.

that of the last. The casualty clearing station, a unit without independent transport, was evidently unsuitable for such capers, and from the first it was wisely decided to send surgical teams to field ambulances. The casualty clearing stations were to follow as closely as possible. The further developments of forward surgical units in the British and American armies is a fascinating study, but another story.

During the war there were developments and improvements, some in forward work and more in the rear areas, but only one epoch-making event—the development of penicillin. Important items were: (i) the control of hospital infection, (ii) the treatment of burns, (iii) the exteriorization of colon wounds, (iv) improvements in reconditioning or rehabilitation, (v) improvements in bone grafting, (vi) plastic surgery.

The treatment of particular types of wounds through the vicissitudes of the two wars and the intervening period is here traced briefly.

Soft-Tissue Wounds.

First let us consider the common or garden wound—the soft-tissue wound—and of course what applies to this as it were basic type of wound applies more or less to all wounds.

In 1914, as in the Boer War, these wounds were dressed. Through-and-through bullet wounds, or even lodging wounds, if not interfered with, frequently healed quickly and well. The wounds produced by shell, mortar, grenade *et cetera* generally became infected, mainly owing to the driving in of dirty clothing, mud and so on, and also owing to dirty fingers, droplet infection *et cetera*. If drainage was good, healing probably took place; if not, there would be abscess formation or septicaemia. The application of local antiseptic agents was of little value. Iodine, carbolic, cresol pastes, all were tried, but they failed to reach the critical area. Any action they had was inhibited by proteins, and they generally did as much harm as good.

Debridement—cleansing and incision for drainage—was the next step. Sepsis continued, and so did the search for the ideal antiseptic. Eusol, Dakin's fluid and other halogens had their trial. The success of the Carrel-Dakin method was due to efficient drainage produced by the prescribed "opening up of all pockets" and by the proteolytic effect of the eusol, which removed the sloughs. Almoth Wright's plea for the free flow of lymph, however produced (salt pack, hypertonic saline solution *et cetera*) was again mechanical drainage. Maggots chewed away the slough and provided drainage. Excision, if good, provided drainage. If excision was very good, why not suture? So suture was tried; but while some cases were successful too many were failures, and the last state was apt to be worse than the first. So secondary suture was instituted and carefully controlled by bacteriological examination. Here surface antiseptics did have a useful role. Many of these wounds were sutured within ten days—what we should now call a delayed primary suture. Flavine—the acriflavine which was used—caused cessation of healing.

That was the position in 1918. In the intervening period between the two wars this method rather fell into abeyance. War wounds are different. The traversing of the tissues by a piece of metal at high speed causes disruption and devitalization of tissues which are not seen in other types of wound. Surgeons found that civilian wounds could be excised and primarily sutured with a high degree of success, and they were loth to believe that they could not apply this treatment to war wounds. Two things militated against them: first, the peculiar nature of war wounds, and second, the necessity for evacuation of the casualties from the forward area, with the sacrifice of the necessary rest. Owing to the increasing popularity of skin grafting, many of these wounds were covered with Thiersch or pinch grafts, when delayed primary or secondary suture should have been carried out. The advantages of a normal skin covering, with a minimum of scar tissue and a consequent rapid regaining of function, are obvious.

A great advance was produced by the systemic administration of sulphonamides. This practically abolished the dreaded streptococcal septicaemia, and in effect it prolonged the period during which primary excision could safely be carried out. As local antiseptics in fresh wounds, the sulphonamides were failures. Their action is inhibited by pus, by proteins and by heavy infection. The British Commission stated that "the local use of the sulphonamides in fresh war wounds has not reduced the incidence nor lessened the severity of infection". "Marfanil", the German sulphonamide, appears to have value as a local antiseptic. Its action is not inhibited by pus and body proteins.

With the decline of the streptococcus the staphylococcus came into prominence—the coagulase-positive staphylococcus A being the worst offender. Sulphathiazole proved to be of value; but this staphylococcus has remained perhaps our worst enemy, and only the advent of penicillin has given us some control over this infection.

Penicillin, of course, has revolutionized the treatment of wounds. The earlier methods of instillation, methods dictated by the necessity for economy, have been discarded. Under the systemic administration of penicillin, with a single local application, most reasonably well-excised wounds may be expected to heal.

Tetanus.

The systematic immunization of the soldiery by the use of tetanus toxoid proved its value in the Spanish war. It does seem that, given satisfactory evidence in the pay-book of immunization, the use of antitetanus serum was unnecessary. Instances of properly immunized men having developed tetanus are exceedingly rare.

Gas Gangrene.

In the Middle East there were few cases of invasive anaerobic infection. Anaerobes were plentiful enough in the Middle East, but there was, particularly in the desert, a low degree of virulence in the coccal infections. Efficient early surgery was available and there was the systemic administration of sulphonamides. It became evident that most cases of invasive anaerobic infection depend upon anaemia of the tissues—an anaemia which can be produced by direct interference with the main vessels or by the pressure of inflammatory oedema. If the wound is excised, if drainage is provided and if coccal infection is minimized, the danger of gas gangrene is small. If the main vessels are injured, and particularly if there are other wounds distal to the vascular injury, there is a considerable risk. This may be reduced by splitting the deep fascia, thus preventing tension and consequent anoxia. A good example is the calf. The value of gas-gangrene antiserum is doubtful. Penicillin has very great value. X-ray treatment (Kelly) is of use in subcutaneous infections.

The conclusions reached are that the invasive anaerobic infections are largely prevented by efficient and early surgical measures. If in spite of these the condition establishes itself, further surgical treatment is the most important weapon, penicillin is next, and serum is some distance behind. The mortality rate now is perhaps 20%.

Compound Fractures.

Compound fracture of the larger bones, and particularly of the femur, was in 1914 a dreadful thing to acquire. Splinting in the field was almost non-existent; the rifle splint and the long Liston splint were the best offering. In the hospitals the Hodgen splint and the Thomas splint were known to some. As early as 1915, Donaldson, sickened by the lack of immobilization, had started plating these early and infected fractures. His results were so bad that disciplinary action was taken against him. It was not until 1916 that the Thomas splint made an appearance in the field, and Sinclair began to resolve some order out of the later treatment. By 1917 his establishment at Wilmereux was in full swing, the Thomas splint in various forms was in general use, and fracture treatment was on its legs. For extension, Steinmann pins had been tried,

but led to too much infection, and Sinclair pinned his faith to glue. Others favoured the caliper.

The early surgical treatment was by this time well understood and efficiently carried out in nearly all cases except those of the fractured femur. To excise satisfactorily a wound involving the femur is difficult and sometimes impossible, particularly a high fracture. Drainage, and particularly dependent drainage, is necessary or the dreaded "sumping" is likely to follow.

By 1918 it was well established that in compound fractures, particularly of the femur, large blocks of undamaged muscle might require removal in order to ensure drainage. Postero-lateral incisions were made and large tubes were inserted to drain the "sumps". Winnett-Orr produced his method of treatment, originally devised for the treatment of osteomyelitis. This was soon applied to the compound fracture and was practised extensively in the Spanish war and extolled by Trueta. An added advantage was that the plaster provided the immobilization necessary for transport.

Excision and the application of plaster were the standard forward surgical treatment at the outset of this war. It has great advantages and great disadvantages, but for transport to the base it was good. All sorts of variations appeared, such as Tobruk Marks I, II and III. The spica was discarded by many as being too difficult of application and too productive of sores. For stationary hospital work the Thomas splint held its own. Kirschner wire traction was universal. The sulphonamides were helping to control sepsis, but secondary hæmorrhage still raised its head.

With the advent of penicillin it was evident that many fractures could be closed early. Even if the skin could not be approximated, the bone could be shut off and the danger of osteitis minimized. In the later stages of the war, when the parenteral administration of penicillin and its insufflation at the time of operation were in use, more than 70% of compound fractures could be closed. The femur still remained "touchy", but even this condition could be tackled if some temporary drainage was provided. The firm pressure dressing, designed to obliterate dead space, began to make its value felt in these procedures.

The Abdomen.

The old tradition said that a man wounded in the belly stood his best chance if he had rest inside and out. "No move, no food, no drink." A few recovered—in the Boer War some 6% or 7%. Probably most of these had no hollow viscus damage, but there are a few proven cases in which this was present. One actually had multiple perforations of the small gut which healed spontaneously, the evidence being found years later at a laparotomy. Other subjects developed faecal fistulae.

In 1914 the edict was "no operation". In 1915, with the upward trend of surgery, tentative efforts to use operation were being made. By 1916, when primary surgical treatment had been established at the casualty clearing stations, there were special establishments for the early treatment of abdominal wounds. At Warloy, behind the Somme, many hundreds of such casualties were subjected to operation with a mortality rate of about 55% or 60%. This figure was not improved upon, in spite of the advent of blood transfusion in 1917.

Twenty years later Jolly had a mortality rate of 50% in a thousand cases of hollow viscus injuries. In Tobruk we could not better this. At Alamein, Giblin, using intensive resuscitation, recorded over 70% recoveries in a small series. In Italy, under harder conditions, the mortality rate was 50%. In north-west Europe the most phenomenal figures were produced, a mortality rate of only 20% being recorded. Our own figures in New Guinea cannot compare with any of these. The mortality rate was 70%.

In 1918 the practice was to establish drainage to the site of colon wounds and to close the abdomen in the case of small intestine and stomach wounds. The wounded were given saline solution and blood intravenously and nothing by mouth until the bowels acted.

Improved methods of resuscitation and intravenous therapy after operation have helped. Stomach suction is of assistance. Exteriorization of colon wounds has probably been an advance, but it is often carried too far. Curiously enough, the colonic anus had a bad reputation in the 1914 war, perhaps because it was reserved for the hopeless case. The intraperitoneal introduction of sulphathiazole is probably worthless. Penicillin has helped, particularly in the healing of the parietal wounds.

The Chest.

The aspiration of hæmorrhages was attempted as early as 1914, but in many cases the condition was too stale to respond. With the extension of surgery in 1916 many primary thoracotomies were performed, but the results were poor, the mortality rate being high. The inevitable swing took place, and by 1918 the motto was "keep 'em dry", by early and repeated aspiration.

Progress in thoracic surgery in the following two decades led to a further outburst of early surgery; but it was soon evident that many more lives were saved and that recovery was hastened by systematic aspiration, started early. The indication for aspiration is not distress; it is the presence of fluid in the chest.

Early operation is advisable in the presence of large foreign bodies, in the presence of continued hæmorrhage, which is always from the parietes, in the presence of foreign bodies or pieces of rib irritating the pleura, and if damage to the left dome of the diaphragm is likely. Later operation is necessary for a clotted hæmorrhax. Diaphragmatic hernia may appear. The removal of intrapneumonic foreign bodies is always a matter for discussion. In 1918 and subsequently it was considered that foreign bodies, unless large, should be left alone if they were not causing signs or symptoms. Penicillin has reduced empyema.

The Head.

Little change has taken place in the surgical treatment of head injuries. Secondary operation may be performed earlier. Penicillin has reduced sepsis.

Nerves.

The conditions with regard to nerve injuries were as in 1918 until quite recently, when the use of electromyography was introduced to distinguish between neuropraxia, axonotmesis and neurotmesis.

Burns.

There were not so many severe burns in the 1914-1918 episode as in the recent war. In the previous war wounds received a thorough cleansing, often with a soft nail-brush, and a picric acid dressing. Then came the day of "Ambrine" and hard upon it the tannic acid treatment. The three-dye treatment was a variant of the tanning process. It was known that saline solution was harmful and that blood was dangerous, and that serum would be the best thing if it was available. The number of "flash" burns which turned up in the desert was a nasty surprise. At first they were tanned, and for flat surfaces tanning is probably as good as most things. But the cracks were terrible. So "Vaseline" was the order of the day. And now a pressure dressing and penicillin seem to be the best treatment. Early epithelialization is essential.

Conclusion.

So much for history, and may we hope that all this is of the past, never to recur. But can the leopard change its spots, or the lion lie down with the lamb? The goats still gambol on Bikini. We must not forget the lessons of two wars, nor must we wait, satisfied with our successes, content to start another struggle with the equipment and organization of the last. We need have no qualms concerning the quality of our medical men, our nurses and our well-trained orderlies. Wisdom lies in unifying the medical services, in developing, training and equipping larger teams, in organizing research on equipment, and in training male nurses.

THE CHEMICAL NATURE OF ALLERGENS: OBSERVATIONS ON "PROTEIN-FREE" PREPARATIONS OF EGG WHITE, LINSEED AND CASTOR BEAN.¹

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UNTIL recently most authorities have held that all allergens are protein in nature, although in 1925 Grove and Coca⁽¹⁾ claimed to have discounted this, and Black and Moore⁽²⁾ strongly maintained that the active fraction of pollen was a carbohydrate. Harsh and Huber⁽³⁾ claimed that Grove and Coca had drawn erroneous conclusions, but the work of Black and Moore does not appear to have been clearly disproved. In 1942 Newell, in reviewing the literature on the chemistry of the allergens of pollens,⁽⁴⁾ indicated that opinion was at variance on this point, although most workers still considered that the active fractions of pollens were proteins.

In 1942 one of us in seeking to isolate the allergen of house dust obtained a remarkably active substance from an aqueous extract of house dust by adsorption on benzoic acid⁽⁵⁾ and this was found to give no qualitative reactions for protein. This finding suggested that it would be of interest deliberately to remove all proteins from extracts of allergens and to see whether the residues showed any allergic activity. Sevag⁽⁶⁾ has described a method for the preparation of "protein-free" solutions under mild conditions and, when this was applied to an aqueous extract of house dust, a product was obtained which gave no protein reaction and which appeared to be almost as active as material obtained by adsorption.⁽⁷⁾ This paper presents brief chemical and clinical observations on products obtained by applying similar treatment to egg white, linseed and castor oil bean, and it will be shown that all three retained intense allergic activity and that 2.0% solutions failed to give any of the usual qualitative reactions for proteins, except that the material from egg white gave a biuret reaction. Before any conclusions can be drawn from these findings, however, it is essential to define some of the difficulties which have caused confusion in the past. Among the more important are the following:

1. Some crude allergens contain several chemically distinct active fractions which react differently in different allergic individuals, all of whom react to the unfractionated substances.⁽⁸⁾⁽⁹⁾
2. The fact that it is impossible at present to separate completely mixtures of large molecules is ignored by some workers.
3. Chemical tests sometimes fail to detect traces of protein *et cetera*, which are easily detectable by biological methods, and certain proteins are not precipitated at all by reagents which precipitate a majority of proteins. For instance, Neuberger *et alii*⁽¹⁰⁾ have pointed out that perchloric acid, which is an excellent precipitant for most proteins, fails to precipitate ovomucoid.
4. Enzymes used to destroy one ingredient in a mixture do not remove the last traces. It is likely that even chemical methods of precipitation fail to achieve complete removal of some organic compounds.
5. It is by no means certain that all pure allergens are antigens, and great care must be used in interpreting the results of sensitization experiments in animals. The allergen may be mixed with a sensitizing substance which is in no way related. However, these experiments are useful in demonstrating the lack of purity in some elaborately "purified" substances.
6. The skin-reacting substance may be only part of the naturally occurring allergen. For instance, it may be similar to the hapten group and not antigenic until it is combined, for example, with a protein or polypeptide.

7. It may eventually be shown that there are marked differences in the chemical nature of different allergens.

8. Even prolonged centrifugation may possibly leave suspended sufficient very finely divided matter to show reactions on very sensitive subjects.

9. No simple method is known for detecting slight differences in activity of two extracts of similar allergens.

Probably the most thorough attempts at isolation and chemical identification of allergens have been made by Spies and his associates working chiefly with material from cottonseed and castor oil beans. These workers claimed that the most important allergens of these two substances are proteins and protein-polysaccharide compounds. However, in their more recent papers they have emphasized the difficulties of accomplishing complete separation of complex organic compounds. In discussing the purification of fractions from castor beans they state: "The solubility curves of CB-60c and CB-65A, Fig. 1 indicated that neither substance was chemically homogeneous."⁽¹¹⁾ (In their series of papers these workers designate the fractions isolated with code letters and figures.)

Coulson *et alii*,⁽¹²⁾ in discussing attempts to purify an active fraction from cottonseed, remark:

The results also emphasize the inadequacy of the usual precipitative methods for complete separation of proteins of such markedly different solubilities as cotton seed globulin and C.S.IA. C.S.IA is very soluble, whereas cotton seed globulin is essentially insoluble in water. Nevertheless, cotton seed globulin preparations purified ten times by ten extractions with distilled water and ten to fifteen subsequent precipitations in water were shown to contain C.S.IA on the order of 0.2 to 0.3 per cent., and, in addition, a trace of another unidentified water-soluble protein. The order of concentration of contaminating proteins observed here are of negligible importance in the usual study of protein chemistry, but because of the extreme sensitivity of the immunologic reactions, these contaminants may assume marked importance in determinations of allergenic activity.

Some authors still maintain that the allergic activity of all samples is due to traces of protein and it is difficult to prove conclusively that no protein is present. However, if the sample is dried and then redissolved to form an almost saturated solution, it is at least suggestive that such a sensitive reagent as sulphosalicylic acid (10%) gives no classical reactions for protein.

Experimental Investigation.

Fifty grammes of sodium acetate dissolved in fifty millilitres of water were added to 100 millilitres of fresh egg white, the pH was adjusted to 4.8 by the addition of 25% acetic acid and a mixture of ten millilitres of butyl alcohol in fifty millilitres of chloroform was added. The mixture was shaken for six hours and placed in a refrigerator overnight. It was then centrifuged and a similar quantity of butyl alcohol in chloroform was added and it was again shaken for six hours. The process was repeated until a sample saturated with picric acid or tested with sulphosalicylic acid (10%) showed no precipitate. Two and a half volumes of ethanol were added and a precipitate appeared after the mixture had stood overnight in a refrigerator. This was centrifuged off and dried by repeated washings in acetone and finally in ether. A pure white powder, readily soluble in water, formamide and diethyleneglycol, was obtained.

In the cases of linseed and castor oil bean, material obtained from an aqueous extract by adsorption on benzoic acid was dissolved in water to form a 2.5% solution and treated as described above.

For chemical and clinical tests 80 milligrammes of each were dissolved in four millilitres of water and the solutions were thoroughly centrifuged. All three samples easily dissolved to form 2% solutions, but the material from linseed produced a slightly turbid solution.

Tests for allergic activity were made by the "scratch" method and no studies have been made using the method of passive transfer.

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Chemical and Clinical Tests with 2.0% Aqueous Solutions of Deproteinized Fractions.

Egg White.—The biuret test showed a marked reaction and the Molisch test gave a faint positive reaction. Sulphosalicylic acid (10%) gave no precipitate, but the 30% precipitant gave a faint precipitate which disappeared on heating and reappeared on cooling. Equal volumes of the deproteinized egg white solution and 30% sulphosalicylic acid were mixed and shaken intermittently at room temperature for forty-eight hours and then centrifuged for an hour at 3,500 revolutions per minute in an angle centrifuge and the slightly opalescent supernatant solution was brought to pH 7.0 with 10% sodium hydroxide. This solution still showed marked allergic activity, as did a sample sealed in a capillary tube and heated to 100° C. for an hour. (It is of interest that ovomucoid prepared by the method of Hektoen and Cole⁽¹⁰⁾ appears to be completely soluble in diethylene glycol and gives no precipitate with 30% sulphosalicylic acid, but otherwise shows many similarities to the product obtained by "deproteinization" of egg white. Both this latter and ovomucoid were found to react strongly on six patients who were hypersensitive clinically and by skin tests to raw egg white, but neither reacted on a ten-year-old boy who was hypersensitive clinically only to the heat-labile portion of egg white. It seems possible that the material obtained by "deproteinization" of egg white consists largely of ovomucoid.)

Castor Bean.—The biuret test gave a negative result and the Molisch a positive result. Sulphosalicylic acid in 10% solution gave no precipitate, but a 30% solution gave a faint opalescence which disappeared on warming and reappeared on cooling. When the solution was treated similarly to the egg white solution with excess sulphosalicylic acid (30%) and centrifuged and neutralized, the allergic activity was not appreciably impaired. Nor was it appreciably impaired when it was heated to 100° C. for an hour.

Linseed.—The biuret test gave a negative result and the Molisch test a positive result. Sulphosalicylic acid (10% solution) gave a faint precipitate which disappeared on warming, but a 30% solution gave a heavy precipitate which disappeared on being warmed and reappeared on cooling. Saturation with picric acid gave a similar precipitate. Samples were treated with excess of both these reagents, left at room temperature for forty-eight hours and centrifuged (in an angle centrifuge at 3,500 revolutions per minute for sixty minutes); the supernatant fluid was neutralized. They still showed marked activity. Heating to 100° C. for an hour did not appreciably impair the allergic activity.

Discussion.

The main object of this paper is to emphasize the fact that when aqueous extracts of some allergens are treated with protein precipitants, there remains in solution much active substance. In view of the difficulties enumerated in the introduction it is impossible to make more specific claims with regard to the absence of protein. Electrophoretic studies will probably give more precise information.

These results, in spite of the above reservations, emphasize the need for a review of current methods of preparation and standardization of extracts of allergens. A knowledge of the chemical nature and stability of allergens should make it possible to prepare and standardize extracts by more direct methods and may perhaps indicate methods of increasing their antigenicity.

Conclusions.

1. Egg white, castor bean and linseed after treatment with several of the classical protein precipitants retain their power to produce marked skin reactions on hypersensitive subjects. However, it must be remembered that certain proteins (for example, ovomucoid) are not precipitated by many of the usual protein precipitants.

2. The difficulty of complete separation of mixtures of complex organic compounds is emphasized.

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References.

- ⁽¹⁾ E. F. Grove and A. F. Coca: "Studies in Specific Hypersensitiveness", *Journal of Immunology*, Volume X, 1925, page 471.
- ⁽²⁾ J. H. Black and M. C. Moore: "Pollen Therapy with Protein-Free Extracts", *The Journal of the American Medical Association*, Volume LXXXVI, 1926, page 324.
- ⁽³⁾ G. F. Harsh and H. L. Huber: "Studies of Tryptic and Peptic Digestion of Extracts of Giant Ragweed Pollen", *Journal of Allergy*, Volume XIV, 1943, page 121.
- ⁽⁴⁾ J. M. Newell: "A Review of Chemical Studies on the Allergen of Pollens", *Journal of Allergy*, Volume XIII, 1942, page 177.
- ⁽⁵⁾ C. Sutherland: "The Preparation of House-Dust Extracts", *British Medical Journal*, September 5, 1942, page 280.
- ⁽⁶⁾ M. G. Sevag: "Eine neue physikalische Enteisungsmethode zur Darstellung biologisch wirksamer Substanzen", *Biochemische Zeitschrift*, Volume LXVIII, 1934, page 419.
- ⁽⁷⁾ C. Sutherland: "The Allergen of House Dust", *THE MEDICAL JOURNAL OF AUSTRALIA*, June 9, 1945, page 583.
- ⁽⁸⁾ C. Sutherland: "Hypersensitiveness to Linseed", *THE MEDICAL JOURNAL OF AUSTRALIA*, May 18, 1929, page 665.
- ⁽⁹⁾ A. H. W. Caulfield, M. H. Brown and E. T. Waters: "Experiments to Determine Whether the Allergically Active Substance in Ragweed Pollen Extract is a Single Entity or Multiple", *Journal of Allergy*, Volume VII, 1935, page 1.
- ⁽¹⁰⁾ C. Neuberg, E. Strauss and L. E. Lipkin: "A Convenient Method for Deproteinisation", *Archives of Biochemistry*, Volume IV, 1944, page 101.
- ⁽¹¹⁾ J. R. Spies, E. J. Coulson, D. C. Chambers, H. S. Bernton and H. Stevens: "The Chemistry of Allergens IX. Isolation and Properties of an Active, Carbohydrate-Free Protein from Castor Beans", *Journal of the American Chemical Society*, Volume LXVI, 1944, page 748.
- ⁽¹²⁾ E. J. Coulson, J. R. Spies and H. Stevens: "The Immunology of Allergens VIII: The Study of the Homogeneity of Cottonseed-Globulin Preparations by Anaphylactic Reactions", *Journal of Allergy*, Volume XVI, July, 1945, page 176.
- ⁽¹³⁾ L. Hektoen and A. G. Cole: "The Proteins of Egg White", *The Journal of Infectious Diseases*, Volume XLII, 1928, page 1.

HORMONES IN GYNÆCOLOGY.

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THE tremendous amount and variety of new work, the general lack of knowledge, the extravagant claims of manufacturing chemists, and the recent return to practice of many medical practitioners who have been out of touch with certain medical advances, make it desirable to clarify our present knowledge of the clinical value of the various hormonal preparations used in gynecology. Since these modern therapeutic agents cannot be employed intelligently and in the best interests of the patient, unless the clinician has some acquaintance with the known facts and theories of the function of certain structures in the female, a brief account of the action of the pituitary gland, the ovary and the placenta will first be given.

The Posterior Lobe of the Pituitary.

The present tendency is to believe that the effects on water metabolism, blood pressure, the intestine and the uterus exerted by the posterior lobe of the pituitary are caused by a single hormone and that pitocin and pitressin are substances which differ from each other and from pituitrin because of the different methods of extraction. Scott-Russell has shown that pitressin is many times more effective as an oxytocic than pitocin when tested on strips of uterine muscle removed at Cæsarean section, so there seems to be no valid reason for employing pitocin in preference to pituitrin, which is more efficient as a uterine stimulant and does not cause more than a slight rise of blood pressure when used to induce labour in a toxæmic patient. Pituitrin will not act as an oxytocic at or near term unless the uterus is first sensitized with oestrogen, which is always present in sufficient amount when the placenta is functioning.

The Anterior Lobe of the Pituitary.

Besides hormones controlling the pancreas, the thyroid, the adrenals and growth, the "master gland" influences

milk secretion by the hormone prolactin, and stimulates the ovary by means of two gonadotrophic hormones known as the follicle-stimulating hormone and the luteinizing hormone. The follicle-stimulating hormone is secreted in gradually increasing amount for some five years before the onset of menstruation, the secretion becoming cyclic during the last year and a half. When the ovary reaches a certain degree of maturity the follicle-stimulating hormone stimulates the growth of a number of Graafian follicles, and finally one ruptures, liberating an ovum. The actual rupture of the follicle sensitized by the follicle-stimulating hormone and the development of the *corpus luteum*, is brought about by the luteinizing hormone. It is thought that prolactin is necessary for the *corpus luteum* to produce its hormone progesterone.

The Nature of Pituitrin and the Gonadotrophic Hormones.

Both pituitrin and the gonadotrophic hormones are protein in nature. They have not yet been isolated in pure form, and their exact constitution is unknown. Preparations are standardized by means of biological tests on laboratory animals.

The Graafian Follicle.

The cells of the Graafian follicle elaborate oestradiol, derivatives from this being oestrone and oestriol. In girls the amounts of these oestrogenic substances gradually increase from the age of eight years till about one and a half years before menstruation begins, when the amount ebbs and flows as the result of the interaction between the follicle and the anterior lobe of the pituitary. This continues throughout the reproductive period, until suitable ovarian follicular material is exhausted (Zondek), when the production of ovarian oestrogen ceases. Oestrogens produce growth and the maintenance of the organs derived from the Müllerian duct—the Fallopian tubes, the uterus and the upper part of the vagina. They promote thickening and maturity of the vaginal epithelium, they are responsible for rhythmical contractions of the Fallopian tubes and uterus, they bring about growth of the duct system of the breast, and they develop the secondary sex characters. The proliferative or preovulatory phase of the endometrium is caused by oestrogens, and they also have an effect on metabolism leading to the retention of calcium. The sudden withdrawal of oestrogens will cause hæmorrhage from a proliferative endometrium, this phenomenon being known as "withdrawal bleeding".

The Nature of the Oestrogens.

The natural oestrogens are steroids, their exact composition is known, and they have been isolated in pure form. For this reason the biological standardization of these hormones is being given up, and dosage according to weight is being adopted; thus 10,000 international units are equal to one milligramme of oestrone.

Stilbæstrol and hexæstrol are strongly oestrogenic substances, which have been obtained by synthesis. The former has an activity comparable with that of oestradiol; but both stilbæstrol and hexæstrol have the great advantage over the natural hormones that they are more effective when given orally and are much cheaper.

Corpus Luteum.

Progesterone is the hormone elaborated by the *corpus luteum* with the help of prolactin. It is responsible for the post-ovulatory, progestational or secretory stage of the endometrium, but only after the uterus has been primed or acted upon by oestrogen. The effect of progesterone on the motility of the Fallopian tubes and uterus is opposite to that of oestrogen; progesterone brings about inhibition. It causes growth of the acinar or secretory part of the breast. It makes the endometrial cells sensitive to mechanical stimulation, which provokes them to react by forming a decidua. Progesterone in sufficient amount prevents ovulation.

Pregneninolone is a synthetic compound with progestational properties. It is effective when given by mouth, but not so effective as progesterone administered parenterally.

Interaction between the Ovarian and Gonadotrophic Hormones.

Each of the hormones of the ovary has an inhibitory effect on the production of gonadotrophic hormones by the pituitary gland. Large or continuous doses of either oestrogens or progesterone depress the gonadotrophic function of the pituitary, and it is probably this action which explains the rhythm of menstruation. The oestrogen formed by the follicle reaches its maximum at ovulation, and this is believed to stop the production of follicle-stimulating hormone and increase the formation of luteinizing hormone (Pfeiffer). When the amounts of both oestrogen and progesterone fall with the retrogression of the *corpus luteum*, the inhibition of the pituitary is removed and it begins again to secrete follicle-stimulating hormone and the menstrual cycle is repeated.

Conditions during Pregnancy.

Oestrogens.

During pregnancy there is a large increase of oestradiol and oestrone in the body; but now it is produced by the placenta, which contains considerable amounts. These oestrogens reach a high concentration at parturition, after which there is a drop to the non-pregnant level. Throughout pregnancy they help to stimulate and maintain the growth of the uterus and mammary duct system, and also they depress the gonadotrophic function of the pituitary.

Progesterone.

When pregnancy takes place the menstrual *corpus luteum* develops still further and produces an increased amount of progesterone during the first four months. The placenta then takes over this duty, but to a much higher level, which is maintained until the end of pregnancy, when the production of progesterone ceases. The function of progesterone during pregnancy is to lessen uterine motility, to aid in the formation of the decidua, to prepare the secretory acini of the breasts, and to inhibit the production of the pituitary gonadotrophic hormones.

Chorionic Gonadotrophins.

The chorionic tissue produces certain gonadotrophic hormones, which can be detected biologically (Aschheim-Zondek test) soon after the embedding of the fertilized ovum. When injected into the immature rat these hormones produce maturation of follicles, hæmorrhage into the follicles and the formation of *corpora lutea*, and because of this they were at first thought to be pituitary in origin. Their concentration in the urine increases at a tremendous rate, to reach a maximum at the end of the second month, when several hundred thousand rat units are excreted per day. The amount then falls to a level from 1,000 to 5,000 units per day, which is maintained till term and then rapidly drops after delivery, when the Aschheim-Zondek test ceases to produce a reaction. The main function of the chorionic gonadotrophins seems to be, at least in early pregnancy, the maintenance of an active *corpus luteum* until the placenta assumes that duty.

It has been mentioned that there is a reciprocity between the oestrogen and progesterone of the ovary and the pituitary gonadotrophins. In a similar manner there seems to be a balancing between the placental oestrogen and progesterone and the chorionic gonadotrophins. The clinical importance of this will be discussed in connexion with the treatment of diabetes.

A distinct gonadotrophin, known as equine gonadotrophin, occurs in the blood of pregnant mares, but is not excreted in the urine. It is not a pituitary hormone, but is thought to be endometrial in origin. In action it is strongly follicle-stimulating, so differing from urinary chorionic gonadotrophin, which is mainly luteinizing.

Lactation.

It is believed that the actual secretion of milk, after the breast has been developed by the placental oestrogen and progesterone, is the result of the action of prolactin from the pituitary. When the inhibitory effect of the

placental oestrogen on the pituitary is removed at delivery, prolactin is produced and initiates lactation, which is continued and increased by the act of suckling.

Some Hormonal Abnormalities.

Amenorrhœa.

Amenorrhœa of endocrine origin may be the result of hypofunction of the thyroid, pituitary (gonadotrophic) or ovary. In each form hypoplasia of the reproductive organs and other signs of immaturity are present, and often adiposity is a feature.

The Menopause.

When the aging of the ovary brings about cessation of menstruation, certain symptoms, mainly vasomotor in nature, arise from the overactivity of the unopposed pituitary gland. The retrogression of the breasts and the atrophy of the reproductive organs and vaginal epithelium are the direct result of the decrease in the amount of oestrogens.

Anovulatory Menstruation.

Occasionally regular hæmorrhages which are not the result of the normal ovulation-corpora-luteum cycle take place, usually at the beginning and end of menstrual life. The follicle matures but does not rupture, and no corpora luteum is formed in that cycle. As the amount of oestrogen drops when the follicle retrogresses, withdrawal bleeding occurs from the endometrium, which is taken to be the normal menstrual flow. The incidence of the condition is unknown, but it is not infrequently found in women complaining of sterility. The hæmorrhage may be normal in amount, but sometimes it is excessive, if the follicle is overactive. Anovulatory menstruation is one of the common causes of functional menorrhagia.

Metropathia Hæmorrhagica.

Metropathia hæmorrhagica follows strong and persistent oestrogenic stimulation of the endometrium causing the typical histological changes and irregular and often profuse uterine hæmorrhages. It is usually the result of failure of ovulation and the persistence of an overactive follicle, any decrease in oestrogen level being followed by withdrawal bleeding.

Hirsutism.

Excessive hairiness with a male distribution occurs in the presence of adrenal tumours, and there is also a tendency towards hirsutism from pituitary dysfunction and hypoovarian conditions; but often hirsutism is seen in otherwise normal women. It is not the result of oestrogen deficiency, but of some androgenic factor probably produced in the adrenals.

The Clinical Use of Sex Hormones.

Although knowledge of the sex hormones is increasing, there are still many problems and phenomena which are unexplained, and often controlled experiments on laboratory animals cannot be reproduced in other species. The popular idea that female endocrinology is an open book and that almost every gynaecological ailment can and should be treated with hormone preparations is to be condemned, for it is only by using these agents intelligently and within their limitations that good results will be obtained.

The Use of Oestrogens.

Menopausal Conditions.—The flushes, giddiness, sweating and mental irritability associated with the menopause are speedily relieved by stilbæstrol, given orally in a dose that will just abolish the flushes. Half a milligramme per day is prescribed, and the dose is either increased or decreased according to its effect on the flushes. The treatment is continued for a few weeks, when an attempt is made to reduce the dosage by instructing the patient to take the hormone on alternate days, or even less often, so that she is at all times using the minimal amount which is necessary for relief. Some patients are relieved permanently after little treatment, but others require large doses given for prolonged periods. Abnormal genital

manifestations, such as senile vaginitis, pruritus and kraurosis may be treated with large amounts of stilbæstrol, up to five to ten milligrammes per day according to the effect, or with a vaginal pessary containing 2,000 international units of the natural oestrogens, one being inserted each night for a few weeks at a time. The results in these local conditions are not always good, and care must be taken to recognize and treat any infection or glycosuria present, and to use other curative methods in addition. The administration of oestrogens in menopausal conditions replaces the lack of ovarian oestrogen, but also has an inhibitory effect on the pituitary. Patients who take oestrogens after the menopause should be warned that they may suffer slight hæmorrhage during the treatment, and especially when the treatment ceases; but the clinician must remember that any hæmorrhage in menopausal women may be a sign of malignant disease.

Gonococcal Vaginitis in Children.—In the treatment of gonococcal vaginitis in children, the introduction of chemotherapeutic agents has reduced the value of the oestrogens, which mature the vaginal epithelium and thereby make it resistant to the gonococcus. A vaginal pessary containing 1,000 international units is inserted each night until one week after smears have ceased to contain gonococci. Often the child's breasts will become enlarged during this treatment, but the enlargement retrogresses when the administration of the oestrogen is stopped.

Primary Dysmenorrhœa with Uterine Hypoplasia.—When ovarian oestrogen is insufficient during adolescence, the uterus remains undeveloped, and often this hypoplasia is associated with dysmenorrhœa. It is therefore rational to attempt to produce uterine growth, hoping that the dysmenorrhœa will be relieved. Stilbæstrol (0.25 to 0.5 milligramme per day) may be given, but only from the end of the menstrual period till the twenty-first day of the cycle, as continuous administration may inhibit the gonadotrophic function of the pituitary. The patient is told that the rhythm and length of the menstrual period may be altered, that she should continue with the treatment for some months, and that a perfect result cannot be expected. Although the condition of many patients is improved, the results are not very satisfactory.

Induction of Labour with Dead Fetus.—Medicinal induction of labour, when the fœtus has been dead for more than a few days is usually unsuccessful because of the absence of placental oestrogen, which is necessary to sensitize the uterus to the action of pituitrin. Success usually follows the administration of stilbæstrol (20 milligrammes twice a day for three days) with the usual medicinal stimulation treatment on the morning of the third day. Should this treatment prove ineffective, the whole routine is repeated some days later.

Pregnancy of Diabetics.—During pregnancy there is a certain relationship between the amount of chorionic gonadotrophin and that of chorionic oestrogen and progesterone. White and Hunt state that in diabetics a rise of gonadotrophin in the blood after the twentieth week to a level of 200 rat units per 100 millilitres predicts premature labour, stillbirth or neonatal death, but that these can be prevented by giving the patient 40 to 120 milligrammes of stilbæstrol and 10 to 40 milligrammes of pregnenolone per day. Quantitative biological tests on the patient's blood are performed each week after the fifth month, and the results indicate when and in what amounts the hormonal therapy is to be used. This does not replace the usual dietary and insulin treatment, which should be carried out rigorously throughout the pregnancy. Remarkable results have been reported, sufficient to justify the adoption of hormonal therapy in this condition.

To Prevent Lactation.—The sudden withdrawal of placental oestrogen at delivery is thought to release the inhibition of the pituitary and allow it to produce prolactin, which initiates lactation. However, if stilbæstrol (one milligramme) is given three times a day for the first seven days after delivery, the inhibition of the pituitary is continued, prolactin is not formed, and lactation does not take place. This is only partly true, and a

perfect result is rarely obtained, unless the fluid intake is limited and there is complete absence of nipple and breast stimulation. The nipples must not be touched, and the breasts should be supported, but no tight binder should be used. Larger doses of stilbæstrol than are recommended here do not give any better result. There is no scientific or clinical reason for using stilbæstrol to stop lactation once it has been established, since the continuance of lactation depends almost entirely on nipple stimulation and breast drainage.

Contraindications.—Oestrogens have been used for a multitude of conditions quite irrationally and with no hope of success. Some of these are hirsutism, sterility, amenorrhæa and uterine inertia. It need only be mentioned that no amount of oestrogen will lessen facial hair. Oestrogen therapy has no place in the treatment of sterility or amenorrhæa, even though hæmorrhage can be induced in any non-menstruating woman (withdrawal bleeding). Uterine inertia, when the placenta is functioning, has never been shown to be the result of lack of oestrogen, and in this condition to give stilbæstrol to a patient who is already saturated with oestrogen shows an ignorance of sex hormone physiology.

The Use of Progesterone.

Functional Uterine Hæmorrhage.—In the anovular hæmorrhage of young girls the *corpus luteum* and progesterone are absent. If the hæmorrhage is excessive, it can often be arrested with an intramuscular injection of five to ten milligrammes of progesterone, which may need to be repeated. Later, when ovulatory cycles become established, the menorrhagia will cease. Progesterone therapy may be used in any functional hæmorrhage, but should not be persisted in if it is unsuccessful.

Threatened and Habitual Abortion.—As progesterone minimizes uterine activity, it may be used in threatened abortion in doses of five to ten milligrammes per day; but it is perhaps wiser to give one injection of ten milligrammes, and if the response is good, to continue. However, if no lessening of the hæmorrhage occurs, it is better to allow what is probably an inevitable abortion to take place. If a patient repeatedly has abortions at the third or fourth month, it may be because there is a diminution in the amount of progesterone produced when the placenta is taking over its formation from the ovary. Theoretically, five to ten milligrammes of progesterone given every five days during this period may be of help, but there is no reason for giving it after the fourth month, when the placenta is producing large quantities. Lack of progesterone as a cause of habitual abortion, if it occurs, must be very rare, and even though an occasional patient seems to benefit, many others attain the same success with no treatment.

In Pregnancy of Diabetics.—The use of progesterone in pregnancy of diabetics has already been mentioned.

Dysmenorrhæa and After-Pains.—Progesterone has been held to relieve dysmenorrhæa and after-pains, because of its effect on uterine motility; but the results have not been good, and in dysmenorrhæa the treatment would need to be repeated each month. Other methods can be used to relieve these conditions and are equally effective.

The Use of Gonadotrophins (Pituitary, Chorionic, Equine).

Many claims have been made that gonadotrophins are of use in the treatment of anovulation, sterility, amenorrhæa, and many other conditions. It has been suggested that ovarian function can be controlled by the pituitary gonadotrophin, that ovulation can be produced by the equine gonadotrophin, and that *corpus luteum* formation can be obtained by the chorionic gonadotrophin. This is not so in humans, and at present the gonadotrophins are useless as clinical agents.

The Use of Androgens.

Testosterone propionate given intramuscularly and methyl testosterone given by mouth may be used in certain conditions, when the oestrogens are contraindicated. They

probably have an inhibitory action on the pituitary. Patients suffering from menopausal symptoms who have hæmorrhages when given oestrogens or who have suffered from breast cancer or endometriosis or who have hæmorrhaging fibroid tumours, may be treated with androgens. The dysmenorrhæa associated with endometriosis is also amenable to androgenic therapy. Testosterone propionate (ten milligrammes) may be given by intramuscular injection every two or three days, and if this dose is not exceeded, signs of masculinization, such as hirsutism, will not appear.

The Use of Thyroid Extract.

Thyroid extract has been used for years in certain gynaecological disorders and is of value. Combined with iron, it may be used in either primary or secondary amenorrhæa, and is often dramatically effective, especially when the amenorrhæa is associated with adiposity. It sometimes benefits patients suffering from functional hæmorrhage. The mode of action of thyroid extract is uncertain in those conditions which are not the result of hypothyroidism; but perhaps it may act as a general tonic and stimulant to the endocrine glands.

THE EPIDEMIOLOGY OF NORTH QUEENSLAND TICK TYPHUS: NATURAL MAMMALIAN HOSTS.

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NORTH QUEENSLAND tick typhus was recognized and described by Andrew, Bonnin and Williams⁽¹⁾ among troops engaged in jungle warfare training on the Atherton Tableland in North Queensland. Two strains of rickettsiæ isolated from cases of the disease have been studied in Australia by Funder and Jackson⁽²⁾ and in America by Plotz, Smadel, Bennett, Reagan and Snyder.⁽³⁾ Andrew and his collaborators briefly discussed the epidemiology of the disease from the aspect of the probable arthropod vector, and produced circumstantial evidence to suggest that adult and larval stages of the tick *Ixodes holocyclus* had transmitted the infection to human beings.

Attempts to determine what animals were natural hosts of infection and to isolate the rickettsiæ from ticks were commenced in the early months of 1945, and this report describes the results of the investigations carried out.

Methods.

Collection of Serum and Ectoparasites.

Captain R. G. Beck, of the 15th Australian Malaria Control Unit, supervised the trapping of animals at three sites: at Wondecia, from the area of rain forest where five of the patients mentioned by Andrew *et alii*,⁽¹⁾ including the two patients (FIK and PHS) from whom rickettsiæ were isolated, were presumably infected; and from two sites at Wongabel, one on the margin of a patch of rain forest, which yielded the small rats and a few of the possums, and the other, in which bandicoots, rat-kangaroos and most of the possums were caught, in open savannah woodland with eucalypts and casuarinas. The animals caught were identified by Captain Beck, with the help in doubtful cases of Mr. H. A. Longman, of the Queensland Museum. Troughton's⁽⁴⁾ descriptions were followed in identifications.

After capture the animals were anaesthetized with ether and their fur was combed with a fine tooth comb to collect the ectoparasites, which were tentatively identified by Major S. L. Allman and Staff Sergeant D. H. Colless, of the 6th Australian Mobile Entomological Section. All ticks taken were forwarded to the Walter and Eliza Hall Institute, Melbourne, for inoculation into guinea-pigs.

The animals were bled by cardiac puncture under ether anaesthesia. The serum was separated from the clot,

¹ Haley Research Fellow, Department of Experimental Medicine, University of Melbourne.

inactivated and placed in ampoules, one drop of 1% "Merthiolate" solution was added, and the ampoules were forwarded to the Walter and Eliza Hall Institute. Major A. A. Ferris, of the Second/Second Australian General Hospital, supervised the collection and dispatch of the serum. As no facilities were available for the systematic inoculation of tissues of captured animals into guinea-pigs, the animals were released in the jungle after they had been bled.

Attempts to Obtain Rickettsiae from Ticks.

Major A. V. Jackson performed the tests made on ticks sent to the Walter and Eliza Hall Institute, and I am indebted to him for details of this work. When a number of ticks collected from several animals were received they were inspected and identified,¹ pooled according to species, and ground in sand and horse-serum and saline solution, and the supernatant fluid was inoculated intraperitoneally into adult male guinea-pigs. In later batches ticks were washed in ether before being ground. Animals were observed for fever and serotal reactions. The tissues of certain of the guinea-pigs were passed into other guinea-pigs, and after the last batch of ticks had been received all remaining animals were given a challenge inoculation with PHS volk-sac emulsion as a test for immunity.

Examination of Serum for Antibodies to the Rickettsia of North Queensland Tick Typhus.

Funder and Jackson⁽²⁾ prepared, from the yolk-sacs of hens' eggs infected with rickettsiae of strain FIK an antigen which gave specific complement fixation with serum from human subjects suffering from North Queensland tick typhus and from guinea-pigs experimentally infected with rickettsiae of strains FIK and PHS. In the present study complement-fixation tests on animal serum were carried out with yolk-sac antigen of strain FIK, the mode of preparation of the antigen and of performance of the test being identical with the methods described by Funder and Jackson.⁽²⁾ The reagents were used in amounts of one standard drop, except the sensitized cells, two drops of which were used. Two full units of complement were employed and fixation was carried out at 37° C.

Results.

Table I shows the numbers of the different species of animals caught at the trapping sites at Wondecla and

¹ It was not possible to have identifications of *Ixodes tasmani* and *Hæmaphysalis humerosa* checked by an entomologist well acquainted with Ixodoidea.

Wongabel, and the numbers of animals of each species on which the various ectoparasites indicated were found. Serum from 111 animals was examined for complement-fixing antibodies, and the numbers of each species from which "+++" or "+++" fixation was obtained at a serum dilution of 1:4 are shown. Serum controls of all specimens recorded as giving positive results showed complete haemolysis at that dilution.

The specimens of serum which gave positive complement fixation at a dilution of 1:4 were tested at higher dilutions. A different batch of antigen, prepared from eggs of the 121st to 127th yolk-sac passages of strain FIK, was used. The ampoule containing one "positive" specimen of serum (from *Isoodon obesulus*) had been broken and the serum could not be tested at higher dilutions. The results of the complement fixation tests are shown in Table II, which also shows where the animals were caught and what were their ectoparasites. Human serum BRY and guinea-pig serum PHS 41 were included as positive controls to indicate the potency of the antigen used. Both gave results similar to those of Funder and Jackson⁽²⁾ for the same types of serum. Four specimens of mouse serum from normal mice and from animals infected with ectromelia and one specimen of normal rabbit serum were included as normal serum controls, and with none did fixation of complement occur.

Twelve batches of ticks, comprising larval, nymphal and adult forms of *Ixodes holocyclus*, *Ixodes tasmani* and *Haemaphysalis humerosa*, and collected from 35 animals, were inoculated into guinea-pigs in an attempt to isolate rickettsiae from them. All tests gave negative results and all the surviving guinea-pigs tested were fully susceptible to a challenge inoculation of PHS yolk-sac emulsion.

Discussion.

The serological studies of Funder and Jackson⁽²⁾ and of Plotz *et alii*⁽³⁾ have shown that the complement fixation test carried out with a suspension of rickettsiae of North Queensland tick typhus (either FIK or PHS strains) is specific and that positive reactions are obtained only with the serum of humans or of animals which have been infected with these rickettsiae. No data are available with North Queensland tick typhus concerning the length of time after infection that complement-fixing antibodies persist in the serum of humans or of animals. Brigham and Bengtson,⁽⁴⁾ who studied the problem as a preliminary step to an investigation of the importance of the wild rat as the reservoir host of murine typhus, found that while in white rats the Weil-Felix reaction fell to normal figures

TABLE I.
Animals Examined, their Ectoparasites, and the Results of Complement Fixation Tests.

Species of Animal.	Place of Capture.	Ectoparasites.																Complement Fixation Tests.			
		Ticks.		Mites.										Fleas.		Lice	Number of Specimens of Serum Tested.	Number of Positive Results at Dilution 1:4.			
				<i>Ixodes holocyclus</i> .	<i>Ixodes nanami</i> .	<i>Hemaphysalis bancrofti</i> .	<i>Trombicula minor</i> .	<i>Trombicula</i> spp.	<i>Leptembius subulifer</i> .	<i>Leptembius</i> spp.	<i>Neochlamis bebbii</i> .	<i>Neochlamis catenulata</i> .	<i>Neochlamis parvipes</i> .	<i>Neochlamis quahberti</i> .	<i>Neochlamis</i> spp.	Parasitic Mites, Various Species.			<i>Pythopappus</i> spp.	<i>Staphanorivius</i> spp.	Near <i>Stethus</i> .
<i>Uromys sherrini</i> (Atherton Uromys).	Wondecla.	9					2		4	4					4	2	3	4		9	1
<i>Trichosurus vulpecula johnstonii</i> (Johnstone's possum).	Wongabel.	17	1													1	1			1	0
	Wondecla.	7	3													2	1	2		6	2
	Wongabel.	35	13	1	3	1	6		6	2						6	1			35	0
<i>Epyrrhynchus rufescens</i> (rufous rat-kangaroo)	Wondecla.	2	1												1	1	1	1		2	1
	Wongabel.	9	3	4	2		1								6	1		8		9	1
<i>Perameles nasuta</i> (long-nosed bandicoot).	Wondecla.	3	1			1								1		1	1	1		3	1
	Wongabel.	2	1		2					1						1	2	1		2	0
<i>Isaodon obesulus</i> (short-nosed bandicoot).	Wondecla.	1																		1	0
	Wongabel.	31	4	2	25	2	6		1	14	7				16	23	12		3	34	2
<i>Melomys cervinipes</i> (fawn-footed melomys).	Wondecla.	6							1	1					3					2	0
	Wongabel.	5		3						1	1				4					2	0
<i>Thylogale cotenii</i> (Cape York pademelon).	Wondecla.	3		1																3	0
	Wongabel.	1																		1	0
<i>Hydromys longmani</i> (Atherton water-rat).	Wondecla.	1									1				1					1	0

TABLE II.
Details of Animals whose Serum gave Positive Results to the Complement Fixation Test.

Key Number.	Providing Species of Serum.	Place of Capture.	Ectoparasites.			Complement Fixation Tests: Serum Dilutions.			
			Ticks.	Fleas.	Mites.	1	2	4	8, 16
2	<i>Perameles nasuta</i> .	Wondecla.	<i>Ixodes holocyclus</i> .	<i>Stephanocircus pygospylla</i> sp., near <i>Stivalius</i> .	Parasit mites.	4	4	4	2
3	<i>Epyprymnus rufescens</i> .	Wondecla.	<i>Ixodes holocyclus</i> .	<i>Stephanocircus pygospylla</i> sp., near <i>Stivalius</i> .		4	4	2	Trace
125	<i>Epyprymnus rufescens</i> .	Wongabel.	<i>Ixodes holocyclus</i> .		Parasit mites.	4	4	3	2
4	<i>Trichosurus vulpecula johnstoni</i> .	Wondecla.	<i>Ixodes holocyclus</i> .	<i>Stephanocircus</i> sp.		4	4	3	Trace
74	<i>Trichosurus vulpecula johnstoni</i> .	Wondecla.	<i>Ixodes holocyclus</i> .		<i>Trombicula</i> sp.	4	3	1	0
24	<i>Uromys sherrini</i> .	Wondecla.			<i>Neoschöngastia hirsuti</i> .	4	3	2	Trace
38 ¹	<i>Isodon obesulus</i> .	Wongabel.	<i>Haemaphysalis humerosa</i> .	<i>Stephanocircus pygospylla</i> sp.	<i>Neoschöngastia cairnsensis</i> .	4	4	4	3
106	<i>Isodon obesulus</i> .	Wongabel.	<i>Haemaphysalis humerosa</i> .		<i>Neoschöngastia cairnsensis</i> .	4	4	4	3
	Human serum BRY.					4	4	4	3
	Guinea-pig serum PHS 41.					4	4	4	2

¹ Serum lost, detailed complement fixation test not made.

within twenty days of infection, complement-fixing antibodies persisted to a fairly high titre for at least ten months. Observations by several other authors (Castaneda,⁶ Johnson and Damon,⁷ and Bengston and Topping⁸) also indicate that in rickettsial diseases complement-fixing antibodies may persist for many months or years after infection.

It seems reasonable to interpret the results of the present serological studies as indicating that, of 111 specimens tested, eight animals of five different species (two each of *Isodon obesulus*, *Trichosurus vulpecula johnstoni* and *Epyprymnus rufescens*, and one each of *Uromys sherrini* and *Perameles nasuta*) had been infected with rickettsiae of North Queensland tick typhus. Ticks collected from seven of these animals were included in batches injected intraperitoneally into guinea-pigs, but no rickettsiae were recovered from them; this suggests that infection had not been present. Five of the eight positive results were obtained from 21 animals caught at Wondecla, and the other three were obtained from 81 animals caught at the Wongabel sites. This difference is significant ($\chi^2 = 6.752$, $P = 0.01$), and supports the conclusion derived from a study of the epidemiology of human tick typhus that the small area of partly opened rain forest known as the Wondecla site is a highly endemic focus of the disease.

Ixodes holocyclus is a three-host tick, which will attack any one of a variety in animals in each of its stages of development. Five of the eight animals from which positive results to the complement fixation test were obtained harboured *Ixodes holocyclus* when caught, and the same species of tick has been taken off some specimens of each of the other two animal species (*Uromys sherrini* and *Isodon obesulus*). No specimens of *Ixodes holocyclus* were taken from any members of the three species of animals from which no positive results were obtained. Whether the common bandicoot tick, *Haemaphysalis humerosa*, is a vector of North Queensland tick typhus in a bandicoot-bandicoot cycle, as it is of Q fever,⁹ must await further experimental investigations.

Both the presumed vector of the human disease, *Ixodes holocyclus*, and most of the natural mammalian hosts have a wide range in eastern Australia, and endemic foci of infection may occur over a much wider area than the Atherton Tableland.

Summary.

One hundred and sixteen native animals were trapped on two sites on the Atherton Tableland, North Queensland, and their ectoparasites and blood serum were collected.

Inoculation into guinea-pigs of 12 batches of ticks of the species *Ixodes holocyclus*, *Ixodes tasmani* and *Haemaphysalis humerosa* collected from 35 animals failed to lead to the recovery of rickettsiae.

Complement fixation tests on the serum of the animals by means of an antigen prepared from yolk-sacs infected with North Queensland tick typhus rickettsiae of strain FIK gave positive results with eight out of 111 specimens of serum. The positive results were derived from animals belonging to the following marsupials: *Isodon obesulus* (short-nosed bandicoot), *Trichosurus vulpecula johnstoni* (Johnstone's opossum), *Epyprymnus rufescens* (rufous rat-kangaroo), *Perameles nasuta* (long-nosed bandicoot); the rodent *Uromys sherrini* (the Atherton uromys) also yielded positive results. These animals are presumed to have been infected at some time with rickettsiae of North Queensland tick typhus.

The majority of the infected animals were collected from a localized area of rain forest near Wondecla, which provided several of the recorded human cases of the disease.

Acknowledgements.

I wish to thank Dr. J. F. Funder for his constant advice and help with the preparation of the antigen and performance of complement fixation tests, and the many army workers enumerated earlier whose cooperative effort made the work possible. The Director-General of Medical Services has given permission for the publication of this paper.

References.

- R. R. Andrew, J. M. Bonnin and S. E. Williams: "Tick Typhus in North Queensland", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, August 24, 1946, page 253.
- J. F. Funder and A. V. Jackson: "North Queensland Tick Typhus: A Comparative Study of the Rickettsia with that of Murine Typhus", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, August 24, 1946, page 258.
- H. Plotz, J. E. Smadel, B. L. Bennett, R. L. Reagan and M. J. Snyder: "North Queensland Tick Typhus: Studies of the Aetiological Agent and its Relation to other Rickettsial Diseases", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, August 24, 1946, page 263.
- E. Troughton: "Furred Animals of Australia", 1941.
- G. D. Brigham and I. A. Bengston: "A Study of the Complement Fixation and Weil-Felix Reactions in Wild Rats as Related to the Isolation of the Virus of Endemic Typhus", Public Health Reports, Volume LX, Number 2, January 12, 1945, page 25.
- M. R. Castaneda: "Studies on the Mechanism of Immunity in Typhus Fever. Complement Fixation in Typhus Fever", The Journal of Immunology, Volume XXXI, 1936, page 285.
- M. B. Johnson and S. R. Damon: "The Serologic Diagnosis of Endemic Typhus. III. The Incidence and Titre of Complement Fixing Antibodies in Random Samples of the Population in Endemic and Non-Endemic Areas", The Journal of Laboratory and Clinical Medicine, Volume XXXI, Number 5, May, 1946, page 551.
- I. A. Bengston and N. H. Topping: "Specificity of the Complement Fixation Test in Endemic Typhus Using a Rickettsial Antigen", Public Health Reports, Volume LVI, 1941, page 1723.
- E. H. Derrick: "The Epidemiology of Q Fever", The Journal of Hygiene, Volume XLIII, 1944, page 357.

Reports of Cases.

SURGICAL TREATMENT OF DEAFNESS: THE FENESTRATION OPERATION FOR OTOSCLEROSIS.

By DOUGLAS G. CARRUTHERS, M.B., Ch.M., F.R.A.C.S.,
Sydney.

SUCH publicity has been given in the lay Press all over the world to the fenestration operation as performed in America that one feels it should interest Australians that the operation has been performed in a number of cases and with gratifying success by an Australian who, though proud to acknowledge as his guiding lights the pioneering work and persevering efforts first of Maurice Sourdille and then of Julius Lempert, has nevertheless devoted his own time and thought to original work along the same lines in Australia for a period of over twelve years. My

to come to lie over the fenestra which you make in the external semi-circular canal. . . . It seems to me that it is an adjacent portion of the skin of the external meatus with only fibrous tissue and perhaps periosteum which could be made to reach the opening in the semi-circular canal. . . . I have always been interested in the fact that the tympanic membrane, and especially the chain of ossicles, form a highly resonant structure. . . . I feel sure that the middle ear with this resonating chain has a lot to do with the acuity of hearing. . . . I wonder whether one of the reasons for the success in your cases might be that you make use of the natural elastic tension of the tympanic membrane? . . . One other point which I intend to try myself . . . is to endeavour to fit some portion of the ossicular chain into the artificial window.

I quote from the copies of these letters, which I wrote because I wish to establish that it is not because of the recent burst of publicity in magazines and in the lay Press that I have taken up this work. I prepared myself for operations of this nature long before the war, and I have now operated on quite a number of patients, naturally with fresh zest since hostilities ceased. I find a certain hesitancy by Australians, especially some medical

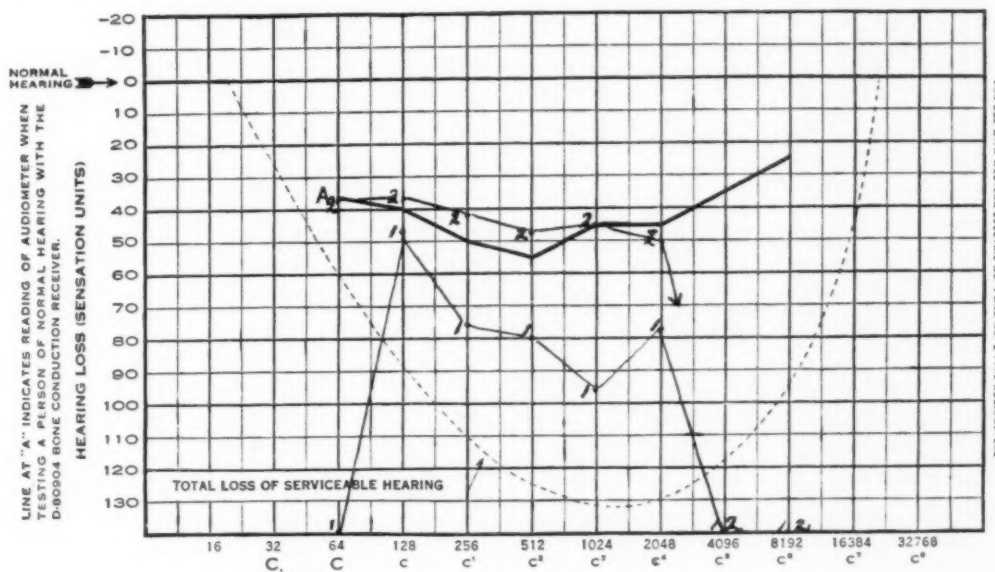


FIGURE 1.

Audiogram of M.G.: 1—1, right ear, December 11, 1945; 2—2, right ear, July 31, 1946.

first inspiration came through the enthusiasm of our late colleague Richard Francis, who had been to see Sourdille at work in about the year 1934. Shortly after this I approached the authorities of the medical school at the University of Sydney, requesting some facilities for carrying out research to devise an operation for the relief of certain types of deafness. As a result I received a Liston Wilson Fellowship, with the aid of which special study was made of the eighth nerve, and with a dissecting microscope and engine-driven burs, I studied fenestration of the inner ear in various regions and from a number of directions.

During this period I corresponded frequently with Lempert in New York. In June, 1939, I wrote as follows: "I have been continuing cadaver practice in the performance of your operations and I hope very soon to commence with the operation for otosclerosis." In March, 1940, again I wrote in the following terms:

I cannot see that you are able to actually displace and stretch the tympanic membrane sufficiently to cause the epithelium covering Shrapnell's membrane

men in official positions, to accept it as fact that an Australian has actually performed this type of operation, and at that without having gone to Lempert in New York to be taught how to do it. My answer to that is simple enough. I started doing the preparatory work at about the same time as Lempert, and I have continued at it ever since, although I claim nothing original for myself and freely acknowledge the inspiration and guidance from Lempert's publications and his letters to me. We both had as a guide the operation of Sourdille, which is still the basis, partly at least, of the approach to the labyrinth. The major problem was how to prevent the fenestra from closing; perhaps the cartilage graft which Lempert has described will prove the answer to that problem. I have used it, and report now the early results in two cases of a series in which I have performed this operation since the war.

Case I.

M.G., a female patient, aged fifty-two years, suffered from deafness, which had commenced first in the right ear nineteen or twenty years earlier, shortly before the birth of

a child, and had gradually become worse. Both ears were affected, the right more than the left. No other ear troubles had been noted. Her mother was deaf and there were said to be others suffering from deafness on the mother's side of the family.

The tympanic membrane was of healthy appearance in both ears. The Eustachian tubes were patent. Bone conduction was greater than air conduction in both ears. The nose and throat were healthy. The audiogram (Figure I) caused a little concern, for in the right ear hearing was

tubes were freely patent. Bone conduction hearing was much better than air conduction hearing. The nose and throat were healthy. Audiograms (Figure II) revealed a loss of 30 to 60 decibels throughout the tone range, the right ear being the worse affected of the two. Bone conduction, with masking of the opposite ear, suggested a practically normal cochlea.

On June 21, 1946, a fenestration operation with cartilage graft was performed on the right ear. Improved hearing was evident on the next day, and much more evident after

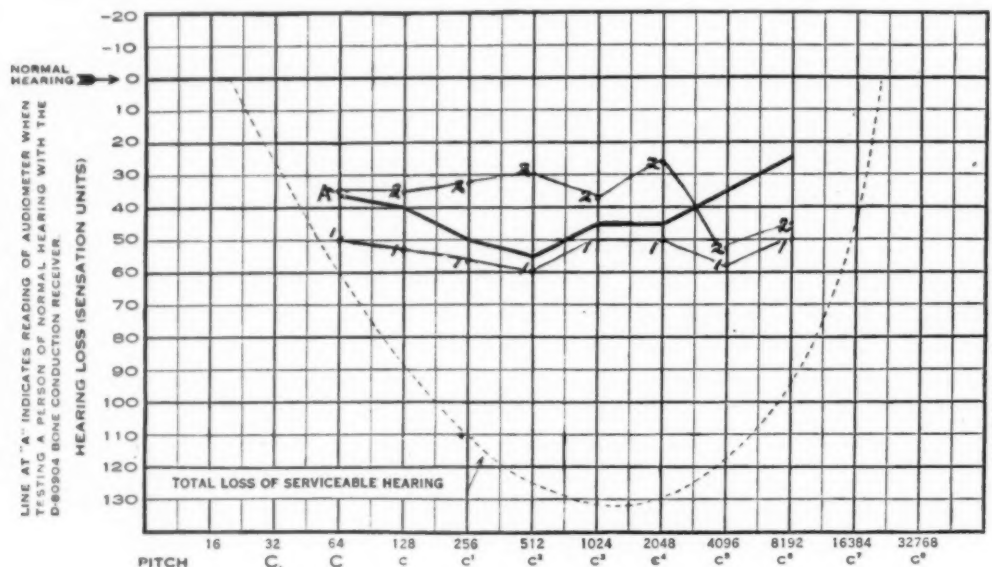


FIGURE II.

Audiogram of C.B.; 1—1, right ear, November 28, 1945; 2—2, right ear, August 1, 1946.

confined to the range from 128 to 2,048 cycles, lower and higher tones not being heard at all by air conduction. By bone conduction the lower range included 64 cycles and the upper range reached 4,096. I felt doubtful of the prospect of operation on the right ear, and was reluctant to attack first the left and more useful ear of a patient aged more than fifty. The use of a hearing aid was declined, and I was requested to try the operation on her more severely affected ear—the right.

A labyrinthine fenestration operation and cartilage grafting were performed on June 28, 1946. Improved hearing was evident on the next day, and has become more pronounced with healing and drying of the cavity, which have been uneventful. The patient now follows conversation readily and she hears the sounds of birds, the door-bell and the telephone, and can enjoy her radio. Her untreated ear, of course, remains as before. Audiograms show that the right ear now hears better within the conversational range than does the left. It is interesting to note that, in spite of the pronounced improvement throughout the tone scale from 64 cycles up to 2,048 cycles, the higher pitches which were not heard at all before operation still remain totally unperceived. As these tones are not required for speech perception, their absence is not missed.

Case II.

Miss C.B., aged twenty-seven years, started to grow deaf when aged fifteen years, the right ear being the earlier involved and the more severely affected of the two. Her mother at the age of fifty-eight years was going a little deaf, and her maternal grandmother was slightly deaf. The patient had had no other ear troubles. The tympanic membranes were of normal appearance. The Eustachian

removal of the dressings on the tenth day. With healing and drying of the cavity her conversational perception has continued to become more acute, so that the patient now has to ask those who previously used to speak to her with raised voice not to do so. The audiogram reveals an average gain of 25 decibels in the speech frequency band.

AN IMMUNE AGGLUTININ IN AN RH-POSITIVE PATIENT.¹

By RUTH A. SANGER and R. J. WALSH,
Sydney.

IN 1941 Levine⁽¹⁾⁽²⁾ reported the discovery of an agglutinin which acted on Rh-negative red cells and on some Rh-positive red cells, but which failed to react with the majority of Rh-positive red cells. Because of these reactions it was called the anti-Hr agglutinin. In 1943 Race and Taylor⁽³⁾ discovered a serum which reacted with the red cells of a larger number of the population (about 80%), including all the Rh-negative individuals. They termed this agglutinin anti-St. Since the latter report there has been much discussion as to the relationship between the two agglutinins. Wiener⁽⁴⁾ believes that the difference in reactions is explained by a difference in titre of the two sera. He points out that the anti-St serum of Race and Taylor acts more strongly on some cells than on others, and that Levine's serum probably reacted only

¹ From the New South Wales Red Cross Blood Transfusion Service.

with the more sensitive cells. However, such a qualitative difference is not in accordance with the views of Race *et alii*.⁽⁶⁾ These workers believe that the anti-St serum contains the γ agglutinin and the anti-Hr serum the δ agglutinin of the scheme worked out by Fisher in 1944.⁽⁶⁾ On the other hand, Levine⁽⁷⁾ has recently stated that the reactions of the anti-Hr serum do not correspond with those expected of Fisher's δ agglutinin, but are identical with those of the γ agglutinin.

Some observations made early in 1945 by the present authors may contribute to the knowledge of these agglutinins. Routine examinations of serum obtained from patients who had received multiple transfusions of blood disclosed a serum containing an agglutinin which is believed to be similar to the anti-St (γ) agglutinin. Samples of serum obtained from this patient before the agglutinin was fully developed agglutinated red cells from a varying percentage of persons, and these variations are of considerable interest. It is believed, too, that this is the first report of an immune anti-St (γ) agglutinin developing as a result of repeated transfusions. Previously reported anti-St (γ) agglutinins have all followed maternal immunization during pregnancy.

Clinical Record.

The patient, a woman, aged seventy-one years, was admitted to hospital on December 4, 1944, complaining of generalized abdominal pain of three days' duration. She was deeply jaundiced and anæmic. The red blood cells numbered 1,740,000 per cubic millimetre, and the hæmoglobin value was six grammes per 100 millilitres of blood. Laparotomy was performed on January 10, 1945, and a distended gall-bladder was removed. The jaundice became more intense and the anæmia decreased only very slowly. Blood transfusions were administered on December 4, 1944, on December 27, 1944, on January 18, 1945, and on January 27, 1945. The amount given at each transfusion was one litre, except the last, at which the amount given was two litres. All transfusions were administered without reactions.

The patient's blood was forwarded for investigation on February 14, 1945, because the last transfusion had not improved the blood picture as much as was expected. The patient was discharged from hospital on April 5, 1945, but was readmitted on October 20, 1945, with an exacerbation of the jaundice and anæmia. Splenectomy was performed on November 21, 1945, and the patient died on December 16, 1945. Further clinical details, although interesting, are not relevant to the present investigation.

Investigation.

In all, five samples of serum were obtained. All possessed strong rouleaux-forming properties, which made interpretation of the results difficult and dilution of the serum necessary. All samples were tested by mixing a drop of the serum suitably diluted with a drop of a weak saline suspension of red cells in a small test tube. It was found that the agglutinin acted most strongly at 37° C., and all mixtures were incubated at this temperature for thirty minutes. Agglutination could sometimes be detected macroscopically, but was never considered to be absent until the mixtures had been examined microscopically. Group O cells only were used, the majority being obtained from a random selection of blood donors, although a few known Rh-negative and Rh-positive cells were used on all occasions. Titrations were performed against the red cells of the same Rh-negative subject on all occasions. Rh tests were performed on all the test cells, but suitable sera were not available at the time to permit the determination of the Rh subgroups.

Results.

The patient's red cells were found to belong to group O and to be Rh-positive. No difficulties were experienced in grouping the red cells.

A sample of serum obtained on February 14, 1945, was tested against 246 group O cells, of which 43 (17.5%) were Rh-negative. Agglutination was obtained with the

red cells from all the Rh-negative subjects and from 95 of the Rh-positive subjects. This represents 138 positive results or 56% of the total number tested. The titre of the agglutinin against Rh-negative cells was 1 in 32.

A second small sample of serum was obtained on February 28, 1945. It agglutinated eight out of 16 cells tested, and had a titre of 1 in 128 against the Rh-negative cells previously used.

The third sample of serum was obtained on March 19, 1945. It was tested against 267 group O cells and produced agglutination with 214 (80.2%). Strong agglutination was observed with 145 samples (54.3%). The remaining agglutinated cells were much less intensely clumped. All the Rh-negative cells (34, or 13% of the total) were in the group showing strong agglutination. The titre of the sample against the same Rh-negative cells was 1 in 512.

The fourth sample, the last obtained for some months, was received on March 26, 1945. The titre of the agglutinin on this occasion was found to be 1 in 256. A quantity of this batch was preserved, in the hope that the agglutinin could at a later stage be correlated with various Rh genotypes. Unfortunately the sample became contaminated with a fungus, and when subsequently tested was found to be inactive.

A further sample of serum was not obtained until after the patient's readmission to hospital. At this time the titre of the agglutinin against the Rh-negative cells previously used was 1 in 16. The rouleaux-forming properties of the serum had increased, and strong non-specific cold agglutinins had developed. It was, therefore, impossible to decide whether the weak reactions were due to specific agglutination, and no estimate could be made of the percentage of positive reactions.

Discussion.

The agglutinin in the serum obtained on March 19, 1944, was thought to be an anti-St (γ) agglutinin. It reacted with Rh-negative cells in every instance, and the percentage of positive reactions (80) obtained with red cells from a random selection of the population is the same as that obtained by the English workers with the original anti-St (γ) serum. This belief has recently been further substantiated, because some cells which were not agglutinated by this serum have since been shown to give negative results with a known anti-St (γ) agglutinin.

It is unfortunate that the various samples of serum were not tested against the Rh subgroups, because the results might have disclosed the nature of the agglutinin in each instance. However, there is no significant difference between the percentage of positive reactions obtained with the first sample of serum (56) and the percentage of cells which were strongly agglutinated (54.3) by the third sample. It is possible, therefore, that the weaker reactions given by the latter sample were missed by the first sample and that the two agglutinins were identical in nature and differed only in strength. If this hypothesis is correct, the results recorded lend support to Wiener's theory that Levine's anti-Hr serum is a weak anti-St (γ) serum.

The antigen which stimulates the formation of an anti-St (γ) agglutinin must be a very weak antigen because of the rarity of the agglutinin. The development of the agglutinin as an immune response to blood transfusions is therefore surprising. In the case reported the agglutinin was obvious fifty-four days after the first transfusion of blood. The fact that other reported samples of the agglutinin have all been the result of a much longer period of immunization—the duration of pregnancy—suggests either that the patient was particularly susceptible or that she had been immunized previously. In the latter event the transfusions would have served as "boosting" doses and caused the progressive increase in the titre of the agglutinin.

Summary.

An anti-St (γ) agglutinin developed in a patient's serum as an immune response to blood transfusions. The significance of the finding is discussed.

Acknowledgements.

The authors wish to acknowledge the assistance given by Dr. B. T. Shallard, Dr. E. B. Durie and Dr. D. Tandy, of the Royal North Shore Hospital, Sydney.

References.

- ⁽¹⁾ P. Levine and S. H. Polayes: "Case Report: An Atypical Hemolysis in Pregnancy", *Annals of Internal Medicine*, Volume XIV, April, 1941, page 1903.
- ⁽²⁾ P. Levine and M. J. Newark: "The Pathogenesis of Erythroblastosis Fetalis", *Journal of Pediatrics*, Volume XXIII, December, 1943, page 656.
- ⁽³⁾ R. R. Race and G. L. Taylor: "A Serum that Discloses the Genotype of Some Rh-Positive People", *Nature*, Volume CLII, September 11, 1943, page 300.
- ⁽⁴⁾ A. S. Wiener: "The Rh Blood Types and Some of their Applications", *The American Journal of Clinical Pathology*, Volume XV, March, 1945, page 106.
- ⁽⁵⁾ R. R. Race, M. McFarlane, D. F. Cappell and R. A. Fisher: "Anti-Hr Serum of Levine", *Nature*, Volume CLV, May 5, 1945, page 542.
- ⁽⁶⁾ R. R. Race: "An 'Incomplete' Antibody in Human Serum", *Nature*, Volume CLIII, June 24, 1944, page 771.
- ⁽⁷⁾ P. Levine: "Anti-Hr Sera", *Nature*, Volume CLVI, October 6, 1945, page 418.

Reviews.

CARDIO-VASCULAR DISEASE.

It is not often that we are able to recommend a book to a general practitioner, consultant physician and medical student, but this is certainly the case with "Cardiovascular Disease in General Practice".¹

The general practitioner will find many answers to his problems and the consultant will find material for his own edification and for the tuition of the students under his responsibility. The student will find ready and readable explanations of physiological and clinical details, which are frequently lost in the greater verbiage of larger books and which he often feels are too elementary to be asked of his tutors.

In making this enthusiastic recommendation we feel at a loss, in admiration of the whole, to select especially outstanding sections. If there are any, they are the chapters on examination of the heart, on heart failure, on congenital diseases of the heart, and the final chapter on the normal heart and some aberrations. These sections particularly contain information in simple yet explicit form, of value to general practitioner and student.

Two points are suggested by specifying those particular chapters. Chapter III on cardiac failure represents the final evolution of the idea of failure of one chamber of the heart and its consequence, following failure of another chamber. This theory has had a chequered career in the years of this century. It is here clearly described and thereby more convincingly established.

Chapter II describes methods of physical examination, and it is possible that here many may not find themselves in agreement with the author. A method of examination is suggested (quoted from *The Lancet*, Volume I, 1938, page 155) in which the examiner follows the blood from the periphery to the right side of the heart, via the lungs to the left, and thence again into the arteries. This sets out a very easy means of establishing in one's mind the physiology of cardiac failure, but the method of inspection, palpation, percussion and auscultation dovetails so well with the examination of systems other than the cardiovascular system that a general practitioner will be loath to change to the new method because of the added time it would entail.

A controversial topic is introduced in Chapter IV, namely, the use of digitalis in cardiac failure with normal rhythm. The use of digitalis in such cases now has many adherents, though few supporters in medical literature. Though it is true that there are few scientific contributions in medical literature which convincingly prove its value, it is pleasant to see an author freely supporting a by now well-established habit.

Minor items only need criticism. These are: the suggestion implied by its mention on page 34 and not on pages 29 to 33 that venesection will benefit right-sided cardiac failure and not left; the omission of oxygen therapy in

failure of the coronary circulation on page 70, and of acute cardiac infarction in the indications for oxygen therapy on page 49; the typographical error on page 75, in which surgical treatment appears to refer to vasomotor angina only and not to all cases of cardiac pain on effort.

One suggestion may be made—that a book of this kind would be improved by a short author's note at the end of each chapter referring the reader to further reliable information on the subject of the chapter.

LECTURES ON MIDWIFERY AND INFANT CARE.

To present the subject of obstetrics in textbook form in a manner suitable for trainee nurses is no simple task. A study of T. F. Corkill's "Lectures on Midwifery and Infant Care" suggests that the author not only has a wide and practical knowledge of his subject, but has also tackled with success the problem of how best to convey that knowledge to the nurse who is undergoing her training in midwifery.¹ Throughout the book there are short sections defining the nurse's responsibility in various circumstances. It is pleasing to find that the role of the midwifery nurse when working in cooperation with a doctor is clearly discussed, as well as that of the midwife who is working alone. In this country the vast majority of nurses who, subsequent to their training, practise obstetrics, do so in conjunction with a medical man.

The text follows the usual pattern, dealing with normal pregnancy and labour, before passing on to considerations of the abnormal. There is a very complete section on infant care, and, the author being a New Zealander, it is not surprising that feeding methods follow the teaching of Truby King. A few references only will be needed to reveal Dr. Corkill's awareness and discrimination in selection of those recent conceptions and developments in the field of obstetrics, which concern the midwifery nurse.

The discussion on nutritional requirements of the pregnant and lactating woman reflects the recent work on this subject. Thus: "It is agreed that unnecessary and deleterious restriction of protein has frequently been advised in the routine ante-natal diet simply as a supposed precautionary measure."

Similarly, reference is made to the detection of pre-clinical oedema by regular weighing of patients in the ante-natal period, to the intravenous use of hypertonic glucose solutions in the treatment of eclampsia, to methods of administration of modern chemotherapeutic agents, and to the use and abuse of antiseptics. A simple account is given of endocrine factors in the reproductive process, of erythroblastosis and of the consequences of vitamin K deficiency in the newborn.

The absence of any illustrations or diagrams in this book, though justified by its title, is rather a disadvantage. This, however, could be overcome if the nurse chose to include as a companion volume Berkeley's inexpensive but excellent "Pictorial Midwifery".

A POCKET OBSTETRICS.

It is always difficult to present the essential facts in a pocket textbook without sacrificing accuracy to brevity; but in "A Pocket Obstetrics" by Arthur C. H. Bell this has been largely achieved.² This small book is intended to help general practitioners and midwives in their work and students in quick revision. The methods mainly follow those of the Queen Charlotte's "Textbook of Obstetrics". The book gives a brief account of normal and abnormal obstetrics, including a section on common conditions found in the newborn.

The description of the conduct of a trial of labour is not adequate, particularly in that no mention is made of the fact that a patient cannot be considered to have had a proper trial of labour until the membranes have been ruptured for at least four hours. However, this is a minor criticism of a good little reference book for those who are not experts in the art of midwifery.

¹ "Lectures on Midwifery and Infant Care: A New Zealand Course", by T. F. Corkill, M.C., M.S., M.R.C.P. (Edinburgh), F.R.C.O.G.; Third Edition, completely revised; 1946. Christchurch, Auckland, Wellington, Dunedin, Invercargill, New Zealand; London; Melbourne, Sydney and Perth: Whitcombe and Tombs Limited. 8½" x 5½", pp. 470.

² "A Pocket Obstetrics", by Arthur C. H. Bell, M.B., B.S., F.R.C.S., M.R.C.O.G., Hon.M.M.S.A.; 1946. London: J. and A. Churchill Limited. 7½" x 4½", pp. 156, with 13 illustrations. Price: 7s. 6d.

¹ "Cardiovascular Disease in General Practice", by Terence East, M.A., D.M. (Oxon.), F.R.C.P. (London); Second Edition; 1946. London: H. K. Lewis and Company Limited. 8½" x 5½", pp. 208, with many illustrations. Price: 12s. 6d.

The Medical Journal of Australia

SATURDAY, NOVEMBER 9, 1946.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

DEAFNESS: SOME CONSIDERATIONS ON TREATMENT AND PREVENTION.

AMONG the branches of medicine in which the doctrine of prevention is often preached rather than practised is that concerned with the organ of hearing. This is partly due to the preoccupation of medical practitioners with other parts of the body and other types of disease; it is also partly due to a lack of appreciation by the general public of the need for attention to the state of the ears. When a defect in hearing becomes manifest it is more often than not due to some infection that has taken place many years before. Once the pain of a middle ear infection has gone and recovery is taking place, little thought is given to the possibility that recovery may not be complete. Even when a discharge comes from the ear it is often accepted as of no great importance. The attention that has been given to discharging ears, and indeed to other disabilities of the hearing apparatus, in applicants for enlistment during the recent war and to members of the forces after their enlistment, has been a useful object lesson. That the experience gained in the services should be applied to civilians has been suggested in a comprehensive and interesting report by F. L. Lederer and W. G. Hardy, who write from the Speech and Hearing Rehabilitation Unit of the United States Naval Hospital, Philadelphia.¹ The general direction of their communication is clear from the title of their article: "Treatment and Training of the Hard of Hearing: A Program of Physical and Psychosocial Therapy."

The report is based on experience gained in the "processing" of almost 3,000 aural casualties. Of 2,500 of these 3,000 persons, 39.4% had some degree of deafness prior to enlistment; 60.6% (1,515 persons) incurred deafness during service. The deafness of 664 of these 1,515 persons was caused by heavy fire; 379 suffered from nerve

deafness and 258 from chronic progressive deafness. Epidemic meningitis was responsible in 28 cases, mumps in six, trauma of the skull in 27, whooping cough in one, machine noises in 54, under-water concussion in eight and chronic suppuration in 90. The aspect of the report to which attention should be drawn may be regarded as the philosophical approach to the problem of retraining the affected person. In answer to the question of what constitutes a person's rehabilitation the definition of the Surgeon-General of the United States Navy is quoted: "All activities and services which may be required to supplement the ordinary or usual therapeutic procedures in order to achieve maximum adjustment of the individual patient either for further military service or for a return to civil life with the least possible handicap from his disability." It is pointed out that in the light of this definition aural rehabilitation involves considerations which lie at the root of a man's psycho-social behaviour. The question arises whether a man with a loss of hearing is different from what he was before he became deaf, and if he is, what can be done about it. Any retraining process must centre round the personality of the person concerned. This fact must be remembered in the rehabilitation of any member of the services who is discharged with a serious disability. A man who has lost a leg, another who has lost an arm or an eye, or one who has suffered a facial disfigurement presents a personality problem as well as one concerned merely with the physical disablement *per se*. As Lederer and Hardy put it—we are not solely concerned with his ability to read speech through muscular cues, nor with his ability to get and hold a job. We are concerned with the psycho-social function of the whole person. A concentration on communicative activities is necessary because they furnish "the core of the function". Lederer and Hardy describe three principal elements in the necessary approach to the problem of the deafened person. The first is expressed in the aphorism that "a man is more important than his ears". The second is the need to arrest deteriorating characteristics and to do everything possible to restore the subject's complete existence. The person concerned "must learn to become not a handicapped person who travels alone, dependent and frustrated, but a 'person who wears a hearing aid', who is in communication with his fellows and who is as capable of economic and social efficiency within the limits of his potentialities as any other man". The third element is the need to help the person concerned to expand certain of his capabilities in order that he may compensate for his hearing loss. Two essential steps towards the goal of a balanced behaviour are described. The first is positive and comprises the development of new abilities, new tools. Fundamental elements in the equipment for normal behaviour are moderate proficiency in speech reading, training in sound discrimination and the supervised use of a hearing aid. The second essential step is negative and involves the understanding and nullification of the adverse effects that are inseparable from serious interference with habits of communication. The subject must learn new ways of getting along in a world that is dependent on communication. He must learn to be quite tolerant of his more fortunate fellow men and must fight the inevitable tendency to become depressed, introspective and negative in his attitude. Lederer and Hardy make many useful observations on hearing aids and also on

¹ Archives of Otolaryngology, May, 1946.

speech reading. (It should be noted that the term lip reading is avoided; in speech reading the kinæsthetic response is recalled and interpreted at the same time as visual cues are received.) A questionnaire was sent to 1,172 patients who had completed the retraining course described by Lederer and Hardy; 508 replies were received and 490 of these are analysed. A total of 94% of the 490 persons were still wearing their hearing aids. In reply to the question how far speech reading had helped in the understanding of conversation, 52% replied "greatly", 35% replied "moderately" and 13% "slightly". The suggestion is made that the kind of retraining used in this rehabilitation of service personnel should be adopted in post-war civilian practice. This is worthy of consideration. Although in certain instances steps of the kind that have been mentioned may be used in some civilian practices, it may be stated that, generally speaking, more attention should be paid to the whole personality of the patient, a hearing aid suited to the patient should be chosen for him, and when loss of hearing is likely to become progressive speech reading should be taught to him. Whether these things should be done in special clinics is a matter for discussion; probably they should. Whether special clinics do the work or not, it will be clear that for many persons some kind of financial assistance will have to be provided, especially in the purchase of a hearing aid. This whole subject is one on which a comprehensive statement by Australian otologists would be valuable.

If we are to advocate and accept the idea that treatment for the hard of hearing should be carried out on certain well-defined lines, we can still be accused of trying to close the stable door after the horse has got away. The best cure for deafness is to prevent it. For this reason we judge that the editor of *Archives of Otolaryngology* chose as the article to follow Lederer and Hardy's communication, a report by D. F. Proctor and W. R. Willard on the work carried out in Washington County, Maryland, in the prevention of deafness in children. This is a subject on which any general practitioner could make a useful statement. Proctor and Willard do not intend primarily to report results, but rather to show how the work in Washington County is carried out and the quantity of work that may be accomplished by such an organization. The work was begun in 1942, and by July, 1945, over 700 new patients had been seen in over 1,500 clinic visits. We do not propose to give any details of the work done except to state that 188 ears with some hearing impairment have returned to normal and 90 with some hearing impairment have improved. It is among the patients with severe recurrent infection of the upper respiratory tract that the work of prevention of deafness has been carried out; 90% of patients affected in this way have shown a decrease in the frequency and severity of infection. Proctor and Willard insist that in work of this kind it is necessary to have an interested and cooperative health department, that equipment must be adequate and that a skilled otolaryngologist must be available. With these basal requirements we shall all agree. It may be held that work on the right lines is being carried out in Australia in the medical inspection of school children. This is true to a certain extent. The trouble is that recommendations about the treatment of school children are made, but that there is no way of seeing that the recommendations are

adopted by the parents of the children. Also in every State of the Commonwealth the staff of medical officers doing the work of inspection is far too small to produce really good results. That must be the subject of a later discussion.

Current Comment.

PENICILLIN IN THE TREATMENT OF AGRANULOCYTOSIS.

THE risk of producing a dangerous degree of leucopenia by the use of thiourea and thiouracil in the treatment of hyperthyroidism has focused more attention on this known complication of certain forms of drug therapy. Amidopyrine once attracted a deal of interest in this direction, but after all it is not a really important or essential drug. More recently the sulphonamides, universally given and, we might almost add, universally taken, have made us realize that with these substances too there is a danger of serious interference with the functions of the blood-forming organs. In the case of the drugs used in the treatment of thyrotoxicosis the problem is perhaps even more difficult, for the patients concerned have been wearing out their metabolic reserves for some time and are balanced precariously on the edge of a crisis which may jeopardize not only progress but even life. Agranulocytosis or even, more accurately, a severe granulocytopenia, is in any case a very serious condition. There is always anxiety in the mind of the physician whether the lag in white cell production, maturation and release will be overcome before the patient's antibacterial resistance is overwhelmed by the sweeping tide of the almost inevitable terminal infection. Penicillin is a logical treatment, for it should confer sufficient powers of resistance on the body cells and fluids to stave off invaders long enough to enable the bone marrow to resume its usual functions.

M. C. Tyson, P. Vogel and N. Rosenthal have described their results in treating with penicillin eight patients who suffered from this dangerous complication in the course of the administration of thiouracil.¹ Five of the patients recovered. One fatal case was that of a patient who succumbed to an underlying cardiac condition, another had only one day of treatment before death, while the third fatal case was that of a woman who apparently had an effective dosage with penicillin, but died with toxic hepatitis. The condition of the patients who recovered seemed to be as bad as that of the patients who died, but once the bone marrow function was restored they made a satisfactory recovery. In several cases blood transfusions were also given. It is worthy of note that in every case thiouracil had been administered for at least five to six weeks before the blood disturbances began. The authors draw attention to a number of reports of recovery of patients who have had agranulocytosis following the administration of sulphonamides and who have been boldly treated with continuing doses of the same drugs. The wisdom of such treatment has been questioned and it has been suggested that recovery was due to the timely rehabilitation of the bone marrow quite apart from any treatment, however heroic. The value of "Pentnucleotide" has also been doubted, and the feeling has been growing of recent years that the treatment of agranulocytosis is a race against time so far as the patient's powers are concerned and that it is hard to estimate the value of any procedures, though it is essential to use all accepted measures vigorously. It is hoped and largely believed that if infection can but be forestalled recovery is possible and penicillin treatment is the treatment of choice, for it is effective in its antibacterial sphere and is non-toxic. Of course it must be remembered that it cannot be expected to be successful against bacteria that are not penicillin-

¹ *Blood*, January, 1946.

sensitive, but in general surely most physicians would feel safer using it than the sulphonamides for this purpose. It would seem that drug toxicity is one of the medical problems of the present and the future, and anything that will help the sensitive haematopoietic system to resist or to overcome the onslaughts on it will be welcome. It is significant that when reduction of the blood elements takes place in the course of a dysplastic blood disease the body seems to have time to compensate for the changes in such functions as resistance to infection. But when chemical intoxication produces these effects, even though there has been a considerable period of sensitization, the evil results come in the end with startling swiftness. The need for keen watchfulness and prompt action is obvious.

THE JUBILEE OF THE MOTOR-CAR.

As a profession of motorists, medical practitioners will no doubt share the general interest and amusement evoked by the recent celebrations in England of the jubilee of the British motor industry. In the latest English newspapers much space has been devoted to the jubilee; in them

Men tell us, they that know the past,
How the proud horse recoiled aghast
The first rude car to see,¹

while photographs depict chiefly a procession of veteran cars, which drove past the King and Queen at Regent's Park. In the procession were cars of the last century bearing the names of Daimler, Wolseley, Rolls, Hillman and Talbot, well known today, besides a good sprinkling of the De Dion-Bouton, predecessor of the Morris, which in the early days of motoring inspired Harry Graham to his happy if ruthless rhyme:

I collided with some "trippers"
In my swift De Dion-Bouton;
Squashed them out as flat as kippers,
Left them "aussi mort que mouton".²

One's laughter "has an echo that is grim" when one is reminded, as our profession so frequently is, of the awful toll of human life taken by the motor-car on the highways today. In this country some five persons are killed on the roads every day and many more are injured. The motor industry in Britain dates its birth to the repeal in 1896 of the *Locomotives Act* of 1865, which limited the speed of automobile locomotives on the roads to four miles an hour and required one of the crew of three to walk not less than twenty yards in front, carrying a red flag. It does no harm to reflect, if we are fain to worship the speed and might of the latest model car, that the *Motor Car Act* of 1896 had earnest opponents, who expressed grave misgivings as to the propriety of licensing individuals to drive massive engines with the power of many horses on the King's highway; certainly the great benefits and convenience that we have derived from the motor-car, which the opposition failed to suppress, have been bought at a terrible cost in human life and limb.

The medical profession in England was quick to see the possibilities of the motor car for professional use. *The Lancet*, which was represented at the *Exposition internationale de vélocipédie et de locomotion automobile* in Paris in 1895, published a glowing account of the new vehicles, "an elegant *vis à vis* upholstered in pig skin", "a nice-looking victoria upholstered in dark green corduroy", "a useful phaeton", together with a good deal of technical information, such as that "the motors range from 2½ to 3½ horse power and the amount of oil consumed is about a quart and a half an hour". It concluded:

With regard to the drawbacks to motor carriages, we have detected very little odour from the petroleum, but we are inclined to think that the complication of the driving mechanism and the amount of technical knowledge required by the driver are underestimated by some. It may be simple enough to work the engine

as long as all goes right. . . . It has also to be considered whether a supply of benzoline . . . can easily be obtained. Considerable vibration is felt in some of the carriages, especially when the carriage is at rest, but the motor is working. But in spite of these and other possible drawbacks we believe that the motor carriage in some of its forms will prove to be admirably suited for the requirements of medical men and will not be long in coming into extensive use.³

As an afterthought it was stated:

The prices at present asked for these carriages will have to be considerably lowered if they are to become universally popular. From £180 to £200 is too high a figure.³

The turn of the century came and a few more years elapsed before motor transport was widely used in this country. In 1907, at the annual meeting of the Civil Ambulance and Transport Corps of the Saint John Ambulance Brigade in Sydney, it was reported amidst applause that a leading citizen had presented the brigade with a new ambulance waggon, "(horse and harness included)". It was the last of its kind, perhaps, but no doubt it dashed through the muddy streets, with its urgent ring-a-ding-ding, no less bravely than its streamlined successor of today with awe-inspiring siren. A few years before this, however, some doctors in Sydney were beginning to use the motor-car on their rounds. Amongst the horse-drawn carriages, strung outside the hospitals, with their grooms, appeared an occasional horseless carriage, with brass headlights gleaming and 70 pounds to the square inch in its pneumatic tires. The motor-car, too, was found a great boon by the country doctor in New South Wales. Sometimes as he filled the priming cups and turned the stiff cranking handle on a freezing night he might wish the horse and buggy days back again; but he could scorch up the miles in the small hours. In the days before the New South Wales *Motor Traffic Act*, 1909, he was allowed some slight latitude in the matter of speed, as witness the following:⁴

An agreement has been arrived at between the Municipal Council of Bathurst, N.S.W., and the local doctors, by which concessions will be granted to the latter as to the rate of speed at which motor cars may be driven through the streets. If the streets are comparatively free from other traffic the motorists may drive up to a rate of fifteen miles an hour, but in cases of emergency, when medical men have urgent calls, no restriction will be placed on them, provided there is no apparent danger or risk to life. All that is required of the doctors is that they should in the event of such a contingency communicate with the local authorities and explain. Prior to this agreement being entered into, three local medics were fined for driving at an excessive rate of speed.

It is not thoughts of speed which preoccupy the country doctor today as he looks forward into the second half-century of motoring. As he comes out in the morning and jumps into his battered pre-war shandrydan, wondering what worn connexion or bearing will give way during the day, what fresh squeak or rattle will be heard, what new short-circuit occur, he thinks no doubt of the formidable cost of the new models, which are beginning to appear on the road, and of whether he will be able to afford a car as strongly made and durable as his present one was, when he is at last allowed to buy one. The cost of new cars, swollen by customs duties and other less identifiable charges beyond all reason, is a serious consideration for him in times of depreciated currency, for his professional emoluments have not increased correspondingly or at all and for years have gone largely not into his own but into the public purse. It can do no harm and may serve to dissipate such gloomy thoughts if our country doctor can try to picture himself a few years hence on his little motor scooter, buzzing comfortably out to see his patients, looking up occasionally with a smile at the sky above him, dark and seething with a torrent of humanity, jet-propelled at supersonic speed!

¹ *Punch*, or *The London Charivari*, August 7, 1946.

² "Ruthless Rhymes for Heartless Homes", 1903, page 62.

³ *The Lancet*, January 4, 1896.

⁴ *The Lancet*, March 7, 1896.

⁵ *The Australasian Medical Gazette*, March 20, 1909.

Abstracts from Medical Literature.

RADIOLOGY.

Spondylolisthesis.

L. H. GARLAND AND S. F. THOMAS (*American Journal of Roentgenology*, March, 1946) state that the X-ray diagnosis of spondylolisthesis should be made only when the vertebral body under suspicion can be shown to be actually displaced anteriorly in relation to the subjacent bone. The essence of olisthesis or slipping is that the whole vertebral body, and not just its posterior surface, is displaced anteriorly. The confirmation of such displacement is aided, in early and minimal cases, by measuring the distance from the anterior inferior margin of the suspected segment to a line drawn perpendicular to the anterior margin of the subjacent uninvolved one (called the perpendicular test line). If the apparently displaced body does not touch this line or lie anterior to it, it is not, in the vast majority of instances, truly displaced. If the displaced body does cross it, a slip is virtually always present. The reason why spondylolisthesis grade 1 is frequently reported, when it is not actually present, is that the body of the fifth lumbar (or involved segment) is foreshortened, so that while its posterior edge lies ventral to that of the subjacent segment, its anterior edge actually does not. It may be stated that, in general, if the fifth lumbar body is normally "rectangular" in shape and proportionate in size to its adjacent segments, there is a slip (olisthesis) only when its anterior margin reaches or passes the perpendicular test line drawn from the first sacral body.

The Significance of the Sacro-Iliac Findings in Marie-Strümpell's Spondylitis.

J. BORAK (*Radiology*, August, 1946) states that the osteosclerosis in the sacro-iliac region seen in the early stages of Marie-Strümpell's spondylitis is confined to the iliac bones, and that the sacro-iliac joints are left free. The findings demonstrate a pathological process of the bone, but not a disease of the joint. The ankylosis of the sacro-iliac joints seen in the late stages of Marie-Strümpell's spondylitis has not been proved to result from a destruction of the cartilages by a pannus, as is the case in other joints affected by the disease. On the other hand, it has its analogy in a process peculiar to the sacro-iliac joints leading to their ankylosis in the course of the ageing process. The sacro-iliac changes do not give rise either to pain or any other clinical symptoms. The symptoms encountered in patients with sacro-iliac findings point to the lumbar part of the spine as the site of origin. X-ray therapy given to the sacro-iliac region is ineffective. It does not alleviate any symptoms, nor does it prevent ankylosis. By contrast, the symptoms around the sacro-iliac joints subside and ankylosis is prevented when the lumbar segment of the spine is irradiated. In view of these facts, the following conclusions may be tentatively drawn. The inflam-

matory process taking place in the spinal joints affected by Marie-Strümpell's spondylitis causes pain, spasm and stiffness. A chronically progressive restriction of mobility results. Such a restriction of the mobility of one part of a body naturally has some adverse effects on the parts with which it is anatomically connected. In the case of the lumbar part of the spine, the longer it is immobilized, the more it becomes functionally integrated into the pelvis. As a result, a bigger block of bones is formed, requiring a stronger support. This induces a chain of physiological reactions tending to restore the weight-bearing capacity of the sacro-iliac junctions, which are severely taxed by the disorder. As the final result of these processes, larger amounts of calcium are deposited in the regions affected, so that the increased stress resting on these pillars is counterbalanced. The symmetry of the sacro-iliac findings seen in the great majority of cases, even in the earliest stages, points in that direction. The *os ilii*, being the largest pelvic bone, is first involved and contributes to this end more than the others. The calcium is first deposited along the joints in the direction of the lines of force, a well-known method of adaptation of the bone to an increased stress. Later, a uniformly dense sclerosis results. Presumably, when the condensation of the iliac bones proves insufficient to increase the weight-bearing capacity of the pelvis, there is sometimes also a condensation of parts of the sacrum and of the bones around the lumbo-sacral junction. Later, a new area of condensation develops in the region of the symphysis as symmetrical as in the sacro-iliac region. When in the course of the disease, owing to the progressing immobilization, a decalcification of the bones sets in, new bone is formed outside the normal skeleton. The osseous ankylosis of the sacro-iliac joints illustrates this way of satisfying the demands for a better support. The bone is formed and deposited in the articular spaces of the sacro-iliac joints, as is the case in the ankylosis of these joints occurring in the course of senile osteoporosis. In the light of this hypothesis, the sacro-iliac findings are not produced by Marie-Strümpell's spondylitis, but merely reflect the occurrence of a pathological process immobilizing the lumbar part of the spine. In other words, they represent not a lesion but a reaction.

Gas Formation in Abdominal Abscesses.

H. STEPHEN WEENS (*Radiology*, August, 1946) states that gas formation in abdominal abscesses does not necessarily indicate the presence of an infection due to *Clostridium welchii* and related bacteria, but may be caused by a variety of organisms. The radiological diagnosis of gas formation is dependent to a great extent upon the localization of the inflammatory process. Gas formation in the retroperitoneal space may have a characteristic appearance. The gas vesicles may occupy the fascial planes, outlining the borders of the retroperitoneal structures, such as the kidneys, adrenals and muscle groups. Gas vesicles localized within the psoas muscles are usually arranged in long

rows parallel to the course of the muscle fibres. This also holds true for infections which spread from the retroperitoneal space into the soft tissues of the thighs and groin, where the gas vesicles may follow the course of fascial planes and muscle bundles. Gas formation in intraperitoneal abscesses is recognized with more difficulty. The differential diagnosis between bacterial gas formation in abscesses and gas localized in intestinal lumina will in many instances be facilitated by the observation that the gas bubbles in the abscess are in an area which is not usually occupied by intestinal loops. Also it may be possible in many instances to identify intestinal loops by their characteristic segmentation and mucosal pattern. Administration of contrast medium by mouth will outline the entire gastrointestinal tract and help to exclude the presence of a fistula. It may be exceedingly difficult to differentiate between gas vesicles localized in an abscess of the abdominal wall and intestinal loops herniated into the abdominal wall. The intestinal loops are often sharply outlined and may maintain some of their characteristic pattern, whereas gas formation in an abscess is characterized by numerous small vesicles which are frequently arranged in clusters. Small gas shadows in abscesses may be easily overlooked, but an examiner who is aware of this phenomenon will recognize them with less difficulty and confirm their presence by repeated examinations of the patient in oblique, recumbent and upright positions and by stereoscopic studies. The observation of gas formation is more helpful than is generally appreciated, and every effort should be made to utilize this phenomenon in radiological diagnosis.

Radiographic Diagnosis of Prolapsed Redundant Gastric Mucosa into the Duodenum.

WENDELL G. SCOTT (*Radiology*, June, 1946) states that prolapse of the gastric mucosa is not rare. In a group of adult males prolapse of gastric mucosa occurred as frequently as gastric ulcer. Prolapse of redundant gastric mucosa produces symptoms that may be suggestive, but not characteristic enough to permit a clinical diagnosis to be made. The condition should be suspected when duodenal ulcer patients have atypical histories, when patients are refractory to an ulcer régime, and when patients have recurrences after being placed on solid foods. The diagnosis of a prolapse of the gastric mucosa is established largely by the X-ray examination. The filling defects are characteristic and should not be confused with those produced by duodenal ulcers, duodenitis or other disorders of the duodenum and pylorus. The typical filling defect in prolapse of the gastric mucosa is a negative "cauliflower-like" defect in the base of the duodenal bulb opposite the pylorus, varying in size and shape during a single examination and on repeated examinations. These defects can be overlooked at fluoroscopy and films should always be made. Fluoroscopy supplemented by the use of "spot films" is the most desirable method of examination. Since large prolapses of the gastric mucosa can produce symptoms, are a cause of gastric hemorrhage and may result in a partial

pyloric obstruction, the radiologist should be on the lookout for them, distinguish them from other duodenal defects, and report them to the referring physician for evaluation. The treatment in early and moderate prolapses is medical until such time as repeated and severe attacks or complications occur. In the large prolapses and in those complicated by repeated hemorrhages or partial pyloric obstruction, surgical measures are indicated. They include excision of the redundant folds of mucosa and usually pyloroplasty.

Hiatus Hernia of the Stomach as a Source of Gastro-Intestinal Bleeding.

ERNEST A. MENDELSON (Radiology, May, 1946) states that hiatus hernia of the stomach can be a source of intestinal bleeding, manifesting itself in hematemesis, melena or microcytic anemia. The cause of bleeding in hiatus hernia is considered to be venous congestion in the herniated portion of the stomach due to muscular compression of the diaphragm. The swollen and congested mucosal layer can easily be traumatized, with the production of superficial bleeding erosions or deeper ulcerations. The accompanying attacks of precordial pain suggesting an acute coronary occlusion or more chronic anginal seizures have been observed by several authors and can well be attributed to the constriction of the herniated stomach by the diaphragm, combined with pressure upon the heart itself.

Clubbed Fingers.

ROBERT CHARR AND PAUL C. SWENSON (*American Journal of Roentgenology*, March, 1946) have studied six cases of bilateral clubbed fingers. In three cases the arterial systems of the hands were injected *post mortem* with barium sulphate suspension and skiagrams were made. In two cases the superficial vessels were made visible by the use of an infra-red filter. In one, urticaria recurred on the palms. The common finding in these cases was increased vascularity about the clubbed fingers, particularly about the ungual processes. The etiology of clubbed fingers is unknown. The prevailing impression seems to be that the clubbing is largely a hypertrophy and hyperplasia of the tissues about the terminal phalanges as a result of increased nutrition caused by an increased peripheral blood flow.

PHYSICAL THERAPY.

Dosage Control in Interstitial Radium Therapy.

J. R. NUTTALL AND F. W. SPIERS (*The British Journal of Radiology*, April, 1946), in a symposium on the subject of dosage control in interstitial radium therapy, point out that in radium therapy, as in X-ray therapy, treatments should be planned beforehand in terms of tumour dose. Statements of dosage to be of any real value for control and for subsequent assessment of results, need to include the minimum dose, the maximum dose and an indication of the general dosage level throughout the treated area. It is not enough merely to attempt to carry

out a prearranged plan. Assessment of the implantation is called for after it has been carried out. Two methods of interstitial dosage assessment have been employed in recent years, namely, post-implantation radiography and condenser measurements at the time of implantation. Radiographic checking has been employed for ten years at the Manchester clinic. It consists of taking two films at right angles to each other, and then by means of a reconstructor, reproducing the implantation in space. Corrections may be carried out after calculation of the dose at various points within the implant area either by modification of the time, or by extraction or insertion of needles. The disadvantages of the method are that the patient has to be moved to a diagnostic X-ray plant, the films are costly, and a considerable amount of work has to be done by the physicist. In the field of dose control, there must be close collaboration between radiotherapist and physicist. Actual measurement of the dosage rate at various points about the tumour whilst the patient is still in the theatre is simpler and more informative than radiography; and the authors have designed a type of interstitial condenser which could be inserted into a trocar-pointed cannula and used for this purpose. The dose rate can be measured by this method in the theatre in about five minutes, and if necessary needles can be rearranged or the overall time altered beyond the planned limits. It is often useful to employ both the radiographic method and the interstitial condenser method in the treatment of individual cases. It is pointed out that dosage control starts at the first consultation with the patient when the decision as to the best method of treatment is made.

Radiological Treatment of Malignant Melanomata.

M. C. TOD (*The British Journal of Radiology*, June, 1946) emphasizes that melanoma is a tumour which must always be treated with the greatest respect. If it is benign it should not be disturbed; if it is malignant the most radical treatment is required. A series of one hundred and seven cases is analysed and the results of treatment are given. It is possible to make a rough estimate that of all patients whose primary growth is diagnosed as malignant melanoma and radically treated, about 30% may be expected to survive five years. If advice is sought by the patient merely for cosmetic reasons, it is best to leave well alone unless there is a history of change in the lesion. The patient must, however, be advised to see his doctor if any injury occurs, if the tumour shows signs of increasing size, if there are new patches of pigment or if it bleeds. Partial removal or such deplorable methods as the use of caustics or ligatures constitute a serious danger. Analysis of the results suggests that there is a significant increase in the proportion of patients in the older age groups alive after treatment, that the results are better in lesions of the head and neck than in those in other sites and that the darker the colour, the more malignant the lesion. In the malignant melanomata of the eye, in the early operable cases the prognosis is quite good. Doubt may remain as to the growth extending along the optic

nerve so that post-operative irradiation is advisable. In the usual form of malignant melanoma, if the clinical factors suggest that the tumour is highly malignant and really wide excision is possible, the patient should be advised that this is best. However, irradiation offers a useful alternative, and as the results in this paper show, can produce a cure in a reasonable proportion of cases. To obtain these cures, however, it is necessary always to give the highest tolerable dosage, taking some risk of necrosis, as malignant melanoma is nearly always radio-resistant, and although it may disappear temporarily at a lower dosage it always recurs. Pre-operative radiation which may increase vascularity is a mistake. The author holds the view that radical surgery should not be followed by prophylactic irradiation, as this may use up tolerance of the normal tissues which may be needed later. In spite of the preference for surgery, radical operation is contraindicated in many cases. Old patients with lesions about the face are better treated by irradiation which will control the growth long enough to allow them to live the rest of their lives in comfort. In cases in which there is doubt whether the growth is true melanoma, carcinoma in an acanthotic wart or a pigmented basal cell carcinoma, irradiation will act as a diagnostic test. Another form is the very extensive papillary black or brown birthmark, which if growing may be restrained by radiation. The author believes that radium implantation should never be used in malignant melanoma because of the danger of trauma. The methods of radiation advocated are radium mould or intensive X-ray therapy.

Radium Treatment of Cancer of the Penis.

Y. L. WICKHAM AND L. DAUVILLIERS (*Journal de radiologie et d'électrologie*, Volume XXVI, 1944-1945, Numbers 3 and 6) state that the frequency of cancer of the penis is particularly high in the Far East where it forms 30% to 40% of all cancers in males. The aetiological importance of phimosis and syphilis is stressed. Three clinical stages of the disease are recognized: early lesions, moderately advanced lesions and very advanced lesions. In the first stage, the end results of surgery and radium are about equal, namely, 30% to 60% five years' cure according to various statistics. Radium should always be the first method of choice, as the penis and a satisfactory method of micturition can be preserved. Surgery can be used generally in case of failure. In the second stage the results of surgery and radium are about equal and radium is therefore generally preferable. The routine radium treatment is by means of a cylindrical Columbia paste mould with a radium-skin distance of 1.0 to 5.0 centimetres and a dose of 6,000r to 8,000r in one to two weeks. Correct dosage calculation is of the utmost importance. Block dissection of the inguinal glands is advised if they are thought to be metastatic. The authors report on 45 cases, 19 of which were in Stages 1 and 2. In five of these cases the patients were treated by surgery and none were cured; fourteen were treated by radium and eight were alive and well after five years. No patients in Stage 3 were cured.

Bibliography of Scientific and Industrial Reports.¹

THE RESULTS OF WAR-TIME RESEARCH.

During the war a great deal of research was carried out under the auspices of the Allied Governments. It has been decided to release for general use a large proportion of the results of this research, together with information taken with former enemy countries as a form of reparations. With this end in view, the United States Department of Commerce, through its Publication Board, is making a weekly issue of abstracts of reports in the form of a "Bibliography of Scientific and Industrial Reports". This bibliography is now being received in Australia, and relevant extracts are reproduced hereunder.

Copies of the original reports may be obtained in two ways: (a) Microfilm or photostat copies may be purchased from the United States through the Council for Scientific and Industrial Research Information Service. Those desiring to avail themselves of this service should send the Australian equivalent of the net quoted United States price to the Council for Scientific and Industrial Research Information Service, 425, St. Kilda Road, Melbourne, S.C.2, and quote the PB number, author's name, and the subject of the abstract. All other charges will be borne by the Council for Scientific and Industrial Research. (b) Those marked with an asterisk may be obtained by approved applicants without cost on making application to the Secondary Industries Division of the Ministry of Post-War Reconstruction, Wentworth House, 203, Collins Street, Melbourne, C.1. Copies of these are available for reference in public libraries.

Further information on subjects covered in the reports and kindred subjects may be obtained by approaching the Council for Scientific and Industrial Research Information Service, the Secondary Industries Division of the Ministry of Post-War Reconstruction, or the Munitions Supply Laboratories (Technical Information Section), Maribyrnong, Victoria.

PB 16793. DÖRING, H., AND KONIG, H. Apoplexy from decompression. No date. 24 pp. Price: Microfilm, 50c.; Photostat, \$4.00.

This decompression apoplexy is caused by aeroembolism in the brain. Since this can end in death, animal experiments were carried out on this topic. The air carried to the brain does not develop in the tissue fluids or in the tissues, as is the case of gas emboli of decompression disease (aeroembolism of American investigators). Rather it is forced from the lungs into the circulatory system while the respiratory passages are closed. According to this explanation, decompression apoplexy is no more an incalculable danger for the stratospheric aviator. It cannot occur if the respiratory passages are open. In conclusion, directions are offered for the crew, and it is demanded that oxygen be inhaled in the combat area and that the positive pressure in the chamber be lowered. Charts and tables and a bibliography are given.

PB 16787. LUTZ, W. Concerning the reversibility of cold-caused "death" of warm-blooded animals. No date. 20 pp. Price: Microfilm, 50c.; Photostat, \$2.00.

This is a translation from a German article and is lacking all the tables and figures mentioned in the text, the translation not being very coherent. Experiments reported are the continuation and at the same time completion of former experiments by W. Lutz and co-workers on the cause and nature of death resulting from exposure to cold, guinea-pigs being used as the experimental animal. For unknown reasons they did not succeed in obtaining the same results with rabbits. The animals were exposed to cold baths until apparent death occurred, after which at varying lengths of time and under varying conditions they were warmed and the cause of delayed death was studied. The following conclusion is drawn: Apparently the reversibility of the cooling-off phenomena is less in respiration than in metabolism and is dependent especially on the body heat. It appears that this contains a very important point for revival from cold. Thus the reason for the slower reaction of the respiration to the application of warmth cannot be sought only in the fact that the head and the respiratory centre are deficient in heat supply when the subject is being warmed in a water bath. It is also present in selective

warming of the head parts, as Wendt and Ruppel could obtain no special success by cervical cord diathermy. The impression is gained that the spontaneous respiration returns independently of the temperature if a well-functioning circulation is present; this again presupposes sufficient lung aeration (artificial respiration) or other insurance of oxygen supply (excess oxygen pressure). The dominant role of artificial respiration in the whole revival problem may be based on similar findings also relative to other kinds of death.

PB 16785. LUTZ, W. On the nature and cause of stopping of the heart upon extreme cooling. No date. 14 pp. Price: Microfilm, 50c.; Photostat, \$1.00.

The beating of the heart stops with extreme cooling, because the beating intervals gradually lengthen to an infinite length while the heart still retains excitability. The stopping of the heart in the cold is to be considered as a completely physiological phenomenon. Rising oxygen pressures displace the tendency of the heart to stop in the direction of lower temperatures. Photostats of charts and bibliography are attached.

SPECIAL REEL for Captain Eley for chemical warfare. Off. Pub. Bd. Report, PB 1686. 1942. 426 pp. Price: Microfilm, \$4.50; Enlargement Print, \$29.00.

Miscellaneous medical publications from *Sitzungsberichte der physikalisch-medizinischen Societät zu Erlangen*, Band 73. 1942. Contains following papers:

1. Lüttge, Werner: Zur Therapie des Abortus febrilis. (On the therapy of abortus febrilis.) 19 pp.

2. Buckel, Walter: Über die Auflösung mehrfacher Nullstellen bei reellen Funktionen einer Veränderlichen und ihren Zusammenhang mit Fragen der lokalen Ordnung, insbesondere mit einer Verallgemeinerung der dupinschen Indikatrix. 11 pp. (Mathematical discussion of differential geometry.)

3. Über Aluminiumstaublung Friedrich Jamin. (On the aluminium-dust lung.) 35 pp.

4. Spirometrische Befunde an Aluminiumstaubkranken Albrecht Engelhardt. (Spirometric findings in patients suffering from inhaling aluminium dust.) 8 pp.

5. Die pathologisch-anatomischen Grundlagen der Aluminiumstaublung. (The pathological-anatomical picture in lungs affected by aluminium dust.) Eugen Kirch. 5 pp.

6. Ergebnisse der Untersuchungen von Arbeitern aus einem Aluminiumstamperwerk. (Results of physical examinations of workers in an aluminium press factory.) F. A. Meyers and W. Kasper. 5 pp.

7. Aussprachebemerkungen zum Vortrag "Aluminiumstaub-Lunge." (Comments on the paper on aluminium-dust lung.) Erich Lunge. 1 p.

8. Die wissenschaftlichen Grundlagen der Behandlung der Erfrierungen mit Kurzwelldurchstrahlungen. (The scientific principles of treating frozen limbs by means of short-wave therapy.) This is a symposium containing the following papers: A. Kälteschäden und Wärmebehandlung mit besonderer Berücksichtigung der Kurzwellen. (Damage done by frostbite and heat treatment using short-wave therapy.) Friedrich Jamin. 24 pp. B. Zur Technik der Kurzwellenbehandlung frostgeschädigter Gliedmassen. (The technique of short-wave treatment for frostbite.) Johannes Pätzold. 9 pp.

9. Die Behandlung und Komplikationen der akuten Erfrierung. (Treatment and complications of cases of acute freezing.) J. Jordan. 10 pp.

10. Pathologisch-anatomische Aussprachebemerkung zu den Vorträgen über Erfrierungen. (Discussion of the pathological-anatomical aspects of frostbite.) Eugen Kirch. 2 pp.

11. Diskussionsbesprechung zu den Vorträgen von Geheimrat Jamin, Dr. Habel Pätzold und Dr. Jordan über Erfrierung. (Comment on the papers by Jamin, Pätzold and Jordan.) Kurt Gross. 3 pp.

12. Discussion zum Vortrag des Herrn Dr. Jordan. (Remarks about the paper by Dr. Jordan.) Dr. Schubert. 1 p.

13. Über die Ursachen der Schlafbewusstlosigkeit. (Concerning the cause of unconsciousness during sleep.) L. R. Müller-Erlangen. 2 pp.

14. Demonstration eines Falles von Schüller-Christianscher Krankheit. (Demonstration of a case of Schüller-Christian disease.) Bruno Fleischer. 6 pp.

15. Zur peroralen Chemotherapie der Urogenitalgonorrhöe. (Oral chemotherapy of uro-genital gonorrhoea.) Helmut Bauer. 2 pp.

16. Fortschrittliche Lagerung und Behandlung Schwerverwundeter. (Progressive changes in the position and treatment of seriously wounded soldiers.) Dr. Heinrich Westhues. 101 pp. This book, the second improved edition, was published in 1944 by the Springer-Verlag in Berlin. The

¹ Supplied by the Information Service of the Council for Scientific and Industrial Research.

fundamental idea brought out is that good, useful war surgery is possible without the facilities of a well-equipped hospital. It shows how to improvise splints, how to make correct fracture bandages, how to change the position of the patient with progressive healing of the wounds. A novelty appears to be a plaster of Paris bandage in connexion with a water pillow. No doubt this book was rendered necessary by the very serious trouble German surgeons encountered in the Russo-German campaigns.

17. *Tropenhygienische Schriftenreihe, Heft 46, 1944. Hippokratesverlag, Stuttgart.* (Malaria in war-time.) (Kriegsmalaria.) 93 pp. A symposium on malaria with the following chapters: I. A general survey of malaria. II. The different types of malaria. III. The clinical aspects of different types of malaria. IV. Therapy. V. Blackwater fever (covers only one page).

18. *Die Leuchtschirmphotographie.* (Photography using a luminescent screen.) Dr. Janker. 1942. Gebr. Schaner, Bonn. 46 pp. This booklet contains the following chapters: I. Photography by means of a luminescent screen as a substitute for the normal X-ray picture. II. The luminescent screen for serial examinations by X rays. III. Photography by luminescent screen as a method of X-ray motion pictures.

19. *Zur Klinik der interstitiellen Pleuropneumonie.* (Clinical aspects of interstitial pleuro-pneumonia.) Dr. Tünnhoff. 22 pp. This is an original typewritten paper apparently not published hitherto. The material is dated from the II Headquarters of the Surgeon General, Dr. Henneberg, September 12, 1944. This article constitutes the findings of a military hospital where an epidemic of pleuropneumonia was discovered in the spring of 1944.

20. *Das Kriegsbedingte, eine neue und kriegsbedingte Form des Ulcus pepticum.* (War ulcers, a new form of ulcer pepticum caused by the war.) N. Henneberg and A. Gzervensky. 18 pp. This also is an original, typewritten paper published by the *Stadtkrankenhaus in Fürth, Bavaria*.

21. *Bilisclectan B-(4-oxy 3,5 diiodphenyl)-a-phenyl-propionsaures Natrium.* (A commercial folder by Schering advertising an X-ray contrast medium for gall-bladder examination.) 2 pp.

22. *Studienplan. A. Vorklinisches Studium. B. Klinisches Studium.* (An outline of the premedical and medical courses for applicants for the rank of army doctors.) 1 p.

BURTON, A. C. *Kaiser-Wilhelm-Institut für Arbeitsphysiologie.* (Physiology of exercise and application to industry, particularly mining.) (BIOS Final Report 53.) Off. Pub. Bd., Report, PB 7911. 1945. 38 pp. Price: Microfilm, 50c.; Photostat, \$3.00.

The principal interest of the institute has been the physiological efficiency of the workman at his work in relation to his industrial output, and the effects upon it of the type of work, working conditions, nutrition and physiological factors. Studies of the caloric content of the food of miners in Germany show that the output of work to be expected will be in direct proportion to the caloric consumption. Work was also done by this institute on ventilation of the lungs as related to oxygen consumption, statistics of weight of population, effects of drugs on efficiency, and protein requirements of the workers. Appendices give a description of the activities of the institute, and a list of published work of the institute and reprints evacuated.

CULLMINE, H. *Pharmakologisches Institut der Friedrich-Wilhelms Universität, Berlin.* Off. Pub. Bd., Report, PB 6662. 1945. 8 pp. Price: Microfilm, 50c.; Photostat, \$1.00.

A discussion of the following problems studied in the institute during the war: smoke clouds of solid substances, toxicology of explosives, blood pigment, toxicology of sulphonamides, enzymes and pharmacological effects, toxicology of "Plasmoquine", tetranitromethane, and intoxication by trichloroethylamine.

FREKHA, FRIEDRICH. *Bericht über die Arbeiten von L. Pauling und Mitarbeitern über die Bildung von Antikörpern in vitro und über Haptene mit zwei und mehr Haftgruppen.* (Report about the work of L. Pauling and collaborators on the formation of antibodies in vitro and on haptens containing two or more reactive groups.) From *Zeitschrift für Naturforschung*, Volume I, Number 1, November, 1945. Off. Pub. Bd., Report, PB 3543. 1945. 3 pp. of galley proofs. Price: Microfilm, 50c.; Photostat, \$1.00.

Eight papers of L. Pauling and collaborators which have all appeared in American scientific journals (*Journal of the American Chemical Society*, Volumes LXII, LXIV and LXV, *Science*, Volume XCIV, and *The Journal of Experimental Medicine*, Volume LXXVI) are abstracted and discussed.

GERMAN ECONOMIC DEPARTMENT, FOREIGN DOCUMENTS UNIT. Summary of reports by Professor Dr. med. habil G. Gaethgens, Kerckhoff Institute, Bad Nauheim: (a) experiments on the

reduction of infant mortality by the use of vitamin K to prevent bleeding; (b) current work of the Kerckhoff Institute; (c) essays, lectures, publications. (C.P.V.A. Report No. 2.) Off. Pub. Bd., Report, PB 8102. 1945. 1 p. Price: Microfilm, 50c.; Photostat, \$1.00.

Dr. Gaethgens has applied to the Health Department of the United States High Command in Germany for assistance in completing mass experiments in the use of vitamin K as a prophylactic for infants. Dr. Gaethgens claims to have discovered a harmless method of giving vitamin K to expectant mothers, and by this a reduction in infant mortality due to bleeding. This report is a one-page summary of an eighteen-page German report which includes a description of the treatment of expectant mothers with the use of vitamin K, the current work of the Kerckhoff Institute, covering electro-physiology of the circulation *et cetera*, and a six-page list of the essays and scientific publications made by Dr. Gaethgens.

HUDGIN, DONALD E., AND VERSOCKI, JOHN A. German smelling tubes for toxic smokes (Riechmittel, Brechampullen) and swabs for skin poisoning (*Tupfer für Hautentgiftung*). (Chemical Warfare Service, Captured Material Technical Report, C.M.T.R. 8.) Off. Pub. Bd., Report, PB 8725. 1944. 5 pp. Price: Microfilm, 50c.; Photostat, \$1.00.

A metal box contains smelling tubes which furnish a soothing odour for nose and throat membranes irritated by toxic smokes, and six absorbent pads to remove vesicants from small portions of the skin. An analysis of each and a photograph are included.

SNYDER, HARRY L. German oxygen therapy set. (Chemical Warfare Service, Captured Material Technical Report, C.M.T.R. 64.) Off. Pub. Bd., Report, PB 8809. 1945. 8 pp. Price: Microfilm, 50c.; Photostat, \$1.00.

This set consists of an oxygen cylinder, an outlet valve, an assembly for hose connexions, an oxygen collection bag, four hose connexions and four masks. The equipment is used for the administration of oxygen in first aid or medical treatment, and compares favourably with therapy sets produced commercially for United States army use. The report contains general description, physical characteristics, and functional characteristics. Photographs are included.

VERSOCKI, JOHN A., AND SCHLESINGER, ALEX. Liquid for first aid for phosphorus burn wounds. *Behandlungsmittel für Phosphorbrandwunden.* (Chemical Warfare Service, Captured Material Technical Report, C.M.T.R. 7.) Off. Pub. Bd., Report, PB 8724. 1944. 4 pp. Price: Microfilm, 50c.; Photostat, \$1.00.

A bottle of liquid used by the Germans for first-aid treatment of phosphorus burns was analysed and its composition found to be 60%, a 1.8% aqueous solution of copper sulphate, CuSO_4 , $5\text{H}_2\text{O}$, and 40% hydrated aluminium silicate. Toxicological tests on guinea-pigs indicate that the liquid provides a means of stopping particles of white phosphorus from burning the skin, but has no therapeutic value.

BROWN, M. H. Visit to the Kaiser-Wilhelm Institut für Medizin, Forschung, Heidelberg, Institut für Chemie. Professor Richard Kuhn. (C.I.O.S. Evaluation Report 384.) Off. Pub. Bd., Report, PB 12644. 1945. 1 p. Price: Microfilm, 50c.; Photostat, \$1.00.

Professor Kuhn has been working for the past six years on a penicillin-like substance said to be very active against *Staphylococcus pyogenes aureus*. It is a yellowish powder, not very soluble in water, more soluble on the addition of boric acid, and said to have toxicity of something in the order of the sulpha compounds. It differs from the sulpha compounds in that it is not absorbed very rapidly and therefore is not excreted very rapidly. The substance is 5,5' dibromo- 2,2' dihydroxy benzil. At present it is being produced in fairly large quantities by Bayers.

BROWN, M. H. Warning phenomenon following immersion in cold water. Oberstabsarzt Dozent Weltz, Institut für Luftfahrtmedizin, München. (C.I.O.S. Evaluation Report 383.) Off. Pub. Bd., Report, PB 12645. 1945. 2 pp. Price: Microfilm, 50c.; Photostat, \$1.00.

Weltz and his group had worked on the resuscitation of airmen who had been immersed in cold water. The chief points advised by Weltz were: (i) optimum temperature for the bath is 45° C. and (ii) warm as rapidly as possible. It was found that the retention of as much clothing as possible added to the chances of recovery.

ERSTICE, WARNER. Manufacturing of surgical adhesive and dressings and artificial limbs by Julius Teufel Company, Stuttgart. (FIAT Final Report 168.) Off. Pub. Bd., Report, PB 13810. 1945. 8 pp. Price: Microfilm, 50c.; Photostat, \$1.00.

The company, though badly bombed, is still operating. It has several plants on the outskirts of Stuttgart engaged in the manufacture of artificial limbs, surgical dressings, stockings for the stumps of limbs, elastic sanitary garments, and adhesives of the heat-sensitive type. Catalogue mentioned is omitted from this copy of the report.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held on July 3, 1946, in the Medical Society Hall, East Melbourne. Dr. F. KINGSLEY NORRIS, the Vice-President, in the chair.

Surgery in Two Wars.

Dr. C. W. B. LITTLEJOHN delivered an address entitled "Surgery in Two World Wars" (see page 659).

Dr. VICTOR HURLEY said that he was particularly interested in the subject of the lecture. He had been associated with Dr. Littlejohn in each war, though peculiarly on neither occasion had they been in the same service. In the first war Dr. Littlejohn was with the Royal Army Medical Corps and Dr. Hurley was with the Australian Army Medical Corps, whereas in the second war he had served with the Royal Australian Air Force Medical Service and Dr. Littlejohn with the Australian Army Medical Corps. Moving around, as he had had to do in the recent war, Dr. Hurley had seen all the medical services, as had Dr. Littlejohn, and they had formed definite ideas on the relative merits of the methods adopted by individuals and by groups in different areas. Dr. Hurley said that while listening with interest and attention to Dr. Littlejohn's sound address, he had selected a few matters on which to comment. It was easier to assess merits in retrospect, but difficult to forecast a few years in advance. The main value of the experiences of war service was the extent to which they could be adapted and used in civil work. Military surgeons had a wealth of clinical material and aid of all sorts available to them. Assistants, money and materials were provided, and they could make observations of real value on a large scale. Unquestionably, for example, the profession's knowledge of the use of penicillin had been expedited by wartime experience, which had been intense and was well documented.

Dr. Hurley went on to say that civil doctors had been greatly respected in the recent war. He had been surprised and delighted to note the many ways in which the non-medical side of the services had come to rely on medical advisers in matters only remotely or indirectly of primary medical interest. The place of doctors in the armed services was now established for all time. There had been few technical improvements in blood transfusion. Even in the previous war there had been few transfusion catastrophes, as Dr. Littlejohn had indicated; the explanation was not easy to determine. In civil cases, direct matching should be carried out, but in emergency a surgeon should be prepared to use a group O (IV) donor if necessary, without special group-testing. Dr. Hurley then referred to the introduction of fluid, and recalled how Starling and Bayliss had stressed the transient nature of the rise in blood pressure, and how Bayliss had added gum acacia as a colloid to improve the position. The introduction of pints of saline solution intravenously could easily be overdone and was not always helpful; of course, the availability of blood, blood serum or blood plasma obviated the difficulty nowadays. There was still, however, a tendency in civil work to "push" fluids uselessly by the intravenous route instead of giving them subcutaneously or by mouth; if fluids were given too rapidly or in too great a quantity, the patients became oedematous and were liable to low-grade sepsis, especially at the bases of the lungs.

With reference to the actual treatment of war wounds, Dr. Hurley remembered the issuing of the Watson Cheyne directions and the return to Listerism; experience had shown that that was not the most effective method of controlling sepsis. He had been especially interested in Dr. Littlejohn's account of the transition in the methods adopted in war surgery of wounds. E. T. C. Milligan and Colonel Gray had pushed the case for wound excision, and it had been justified by results. Carrel-Dakin treatment had enjoyed a temporary reputation when combined with thorough wound excision; but the improvement was ultimately recognized to be due to proper drainage rather than to the special qualities of the Carrel-Dakin solution. Dr. Hurley commented that even in compound fractures, after resuscitation of the patient excision of the wound and effective drainage were essential principles. Speaking of primary suture, he went on to say that surgeons would always be found who would toy with the idea of sewing up the wounds; the notion was constantly being revived, but the tragedies of primary suture usually checked those enthusiasts. With penicillin it would be tried again, and perhaps justifiably. Never-

theless, delayed suture was safer and not much time was lost; drainage was still an essential principle. Most surgeons in Melbourne preferred to use the Thomas splint for lower limb injuries other than those around the hip joint itself; that preference had probably been confirmed by experience in the recent war. Dr. Hurley agreed with Dr. Littlejohn that Maurice Sinclair had not been given enough credit for his fracture work in the previous war. He thought, however, that skeletal traction procedures had probably become reasonably safe, since penicillin could be given as a safeguard against sepsis. Splinting with plaster of Paris was becoming better understood; the French were always keen on it, and the results of its use by them in the 1914-1918 war were appalling before the general practising of wound excision. Trueta, in the Spanish Civil War, had restored to favour closed plaster of Paris treatment. It was to be noted, however, that he worked in Barcelona, a city comparable with Melbourne, with good hospitals, many ambulances and good roads, and no scarcity of suitable appliances and equipment; better results would be expected, for example, in Melbourne under wartime control than in a place such as New Guinea under front-line conditions.

Commenting on the treatment of burns, Dr. Hurley said that he had been an active participant for twenty-five years or more and could testify that saline baths were used when he was a resident medical officer. The method had gone right out of favour because the tissues became sodden, but the idea was revived on a large scale during the recent war, though he conceded that it was used more intelligently than in the old days. The same applied to tissue coagulants. Milligan was probably one of the first to introduce coagulation treatment; as a resident medical officer at the Children's Hospital, Melbourne, in 1910, he had published an article on the advantages of treatment of burns with alcohol; the raw area was sealed over with methylated spirits, but the dressings were painful and it was usual to do them while the patient was under general anaesthesia. Years later, Davidson, of Detroit, had introduced the tannic acid treatment, which had a wide vogue and was very valuable if due attention was paid to desiderata and precautions. In Dr. Hurley's opinion pressure dressings and the parenteral administration of fluids could not be expected to take the place of coagulants in the treatment of severe burns. Coagulation treatment had certainly reduced the mortality rate from severe and extensive burns.

Referring again to the use of plaster in fractures, Dr. Hurley said that if the free escape of fluid was ensured, the Winnett Orr or Trueta closed non-padded plaster method had its uses, and further, it should be remembered that the same method was used for simple fractures, but it could be disastrous. A note of warning needed to be sounded; the risk of endangering the circulation was considerable. Dr. Hurley then expressed to Dr. Littlejohn his personal thanks for assistance and guidance to the Royal Australian Air Force Medical Service during the war. Dr. Hurley had always been crossing his tracks, and had always found appreciation of his advice and assistance by surgeons of the various defence medical services.

Dr. IAN WOOD said that he wished to congratulate Dr. Littlejohn on his work during the war. The physicians also admired, valued and appreciated his help and knowledge, and many had formed an affection for him; his sympathetic understanding of difficulties encountered was almost as valued as his professional advice.

Dr. B. K. RANK said that, in his opinion, Dr. Littlejohn's lecture should be made compulsory reading for medical students. With special reference to burns, as his name had been mentioned, he wished to point out that when one was working under civilian conditions conclusions reached under less favourable service conditions did not necessarily apply. Undoubtedly, to close an infected burn was very wrong. He also wished to make it clear that he did not consider that there was such a thing as the saline bath treatment for burns; the saline bath was used merely to facilitate grafting and prepare the skin for it; coagulants took too long to remove, and tanning should not be employed if it was not necessary, as it impeded the stage of preparation for skin replacement. Dr. Rank added that under modern civil hospital conditions there was seldom any need for tissue coagulation; at best it added a week to the period before skin replacement could be undertaken.

Dr. NORRIS, from the chair, said that Dr. Hurley had raised an interesting point on the position in the services attained by the medical officers. The late revered General Vasey at the planning before Shaggy Ridge had asked to be informed of the proposed positions to be allocated to the surgical teams and had brought them much nearer. Dr. Norris

mentioned this incident to illustrate the fact that a divisional commander had learned to demand the right surgical treatment for his men, and was even prepared to override local medical opinion when convinced of the soundness of the advice of consultants such as Dr. Littlejohn. The inspiration of the consultants was also much appreciated by the medical officers, and in the discussions led by them at the end of the day's work the officers obtained valuable surgical tuition. Principles were not always recognized and applied faithfully by enthusiastic youths, but experience always led back to the faithful use of principles.

Dr. Littlejohn, in reply, expressed thanks for the favourable reception given to his paper. He said that as the field was so large, he had had to curtail his review of war surgery.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held on June 12, 1946, at the Children's Hospital, Melbourne, Dr. A. P. DERHAM, the President, in the chair. Part of this report appeared in the issue of November 2, 1946.

Neuromyelitis Optica.

DR. E. GRAEME ROBERTSON showed first a boy, aged seven years, who lived in a remote country district where human contacts were few. On April 19, 1946, he suffered from a cold with slight malaise and remained in bed for one day. On April 28 he noticed a tickling sensation over the skin of his right calf. Although at first the sensation merely amused him, later in the day it spread to the dorsum of the foot and to the medial surface of the upper part of the thigh and caused him to cry and to scratch at the skin. On the next day he limped slightly on the right leg. Three days after the onset he again complained of tickling over the right calf. During the next night he noticed similar tickling at the back of the left leg. The weakness of the right leg slowly became more obvious. During the seventh day he complained of tickling in the right armpit and under the shoulder-blade. Otherwise he seemed well, but was disinclined to walk. Nine days after the onset both lower limbs were weak, the right being weaker than the left. It was noticed that he could not see distant objects nor recognize the colour of traffic-control lights. He was examined at this stage by Dr. H. Boyd Graham, who had provided the early history. The patient was admitted to hospital under the care of Dr. J. W. Grieve ten days after the onset. His temperature was 98.4° F. The pulse rate was 128 per minute and the respirations numbered 28 per minute. There was considerable weakness of the right lower limbs. The knee and ankle jerks appeared to be slightly diminished. The abdominal reflexes were absent and the plantar reflexes were extensor in type. The weakness of the lower limbs increased, until a week after the child's admission to hospital (eighteen days after the onset) they were powerless. At this stage the visual acuity was $\frac{1}{200}$ in each eye, estimated by the Snellen types, the reduction being due to central scotomata. Slight haziness was present at the nasal edge of the left optic disk; otherwise the cranial nerves appeared normal. No loss of power or of coordination was detected in the upper limbs. The lower intercostal muscles appeared to contract poorly and the muscles on the right side of the abdomen were weak. The patient was unable to move the lower limbs. The deep reflexes were generally poor. The superficial abdominal reflexes were absent and the plantar reflexes were extensor in type. Hypoesthesia and hypoaesthesia were present with inability to feel small differences of temperature below the sixth thoracic dermatome. The child was unable to feel vibration over bony points of the lower limbs and could not appreciate slow movements of his great toes. However, sensation was much less affected than motor power.

Dr. Robertson went on to say that investigations included lumbar puncture. The initial pressure of the cerebro-spinal fluid was 210 millimetres of water; this figure was partly due to straining. The response to compression of the jugular veins and to release of pressure was normal. The fluid was unfortunately blood-stained. It was estimated that there was a relative increase of the leucocyte content to the extent of 60 per cubic millimetre, four-fifths being polymorphonuclear cells and one-fifth lymphocytes. No further examination of the cerebro-spinal fluid was made because

of the heavy contamination with blood. The blood did not react to the Wassermann test. Subsequently considerable improvement occurred. At the time of the meeting, eight weeks after the onset, both optic disks were pale, although the vision had improved. The visual acuity was now $\frac{1}{200}$ in the right eye and $\frac{1}{400}$ in the left. Fine nystagmus was observed on left lateral deviation of the eyes; otherwise the cranial nerves were normal. No abnormality was detectable in the upper limbs. The abdominal muscles were generally weak, especially on the left side. In the lower limbs all movements had returned, but were weak. At the hip joints flexion and abduction were very weak. Flexion and extension of the right knee were much weaker than those of the left, and dorsiflexion of the ankle was much weaker on the left side than that on the right. Movements of the lower limbs were ataxic. The deep reflexes in the arms were of normal activity, the knee and ankle jerks were hyperactive. Patellar clonus was present on both sides and clonus at the left ankle joint. The upper abdominal reflexes could be elicited; the plantar reflexes were extensor in type. Slight hypoaesthesia and hypoaesthesia were present over the same area as before and appreciation of position and passive movement of the great toes was poor. Dr. Robertson said that it was of considerable interest to notice that no disturbance of the control of micturition had been noticed. Five weeks after the onset the patient began to pass urine frequently and complained of much scalding pain during micturition. Microscopic examination revealed many pus cells. His temperature since then had risen each evening to 99° or 100° F. The pulse rate varied between 88 and 124 per minute.

Dr. Robertson's second patient was a boy, aged five years, who had been admitted to the hospital under the care of Dr. W. W. McLaren. On February 24, 1946, at 3 p.m., he complained of headache and soreness above his eyes. He was fretful and in the evening was restless and hot. On the next day he complained of pain in the right calf and lay in bed alternating between sleep and grizzly listlessness. Subsequently his condition improved, until four days after the onset he was up and about, although lacking in energy. Two days later his right leg began to give way underneath him, and after he had been for a walk he complained of pains over both lower limbs, worse on the right side. The weakness of the right leg increased, and nine days after the onset contact with the skin of the lower limbs caused him to flinch and cry. There was no disturbance of micturition. On the next day it was seen that the right corner of the mouth moved slightly less than the left and that the right deltoid was weak. He was unable to sit up unaided and the lower abdominal muscles were weak. Flexion of both thighs was weak, and he was unable to lift the right leg against gravity. Abduction of the right thigh was impossible, and that of the left thigh very weak. Adduction on both sides was weak, extension being the strongest movement. Flexion of the right knee was extremely weak, extension being less affected; on the left side the power was somewhat better. Dorsiflexion of the right foot was weak, other movements at the ankle joints being of fair power. The deep reflexes in the arms were normally active, the knee and ankle jerks were increased. The upper abdominal reflexes were diminished, the lower absent. The plantar reflexes were extensor in type. No sensory loss was detected. There was no limitation of movement of the spine. The temperature was 98° F. (occasionally during the illness it reached 99° F.), the pulse rate was 100 per minute, and respirations numbered 26 per minute. The cerebro-spinal fluid contained thirteen lymphocytes per cubic millimetre. The pressure was normal; but there was no response to jugular compression. Radiographs of the spine revealed no abnormality. During the next few days the muscles of the right shoulder became weaker. The intercostal muscles became very weak, respiration being chiefly carried out by the action of the diaphragm. The lower limbs were completely paralysed, and priapism was present. It seemed wise to exclude the possibility of spinal compression. However, the response to Queckenstedt's test was normal, and oxygen passed upwards throughout the spinal theca without interruption.

Dr. Robertson said that nineteen days after the onset the patient began to move his lower limbs; but at this stage his voice became slow and thick with a nasal quality, and he had some difficulty in swallowing. The cerebro-spinal fluid at this stage was normal (no cells were seen, and it contained twenty milligrammes per centum of protein). The Wassermann test failed to produce a reaction in the blood or the cerebro-spinal fluid. Ten days later the speech was much worse and swallowing more difficult. Between meals the patient dribbled constantly. On examination at this stage the right optic disk was found to be pale, and

the pupil reacted poorly to light. Facial movements were poor on both sides, all muscles being weak. Bilateral palatal and pharyngeal weakness was present, without sensory loss. The pyramidal involvement was lessening. Six weeks after the onset the child was able to swallow solids more easily, but fluid ran out of his mouth when he tried to drink. Speech was nasal in quality. He was walking better, but still had bilateral pyramidal signs. He cooperated better during examination, and slight sensory loss was detected below the first lumbar dermatome. He was now aware that he could not see properly with his left eye. Two months after the onset speech and the act of swallowing were apparently normal and he was able to run. At the time of the meeting (four months after the onset) the right optic disk was pale. The visual field was of normal extent, but central vision was greatly depressed. He was able to count fingers with this eye. The vision of the other eye was normal. The right corner of the mouth moved less well than the left, but there was no detectable loss of power elsewhere. The knee and ankle jerks were very active, and the plantar reflexes were extensor in type. The absence of any evidence of interference with the control of micturition was again a striking feature. This implied that the descending tracts subserving inhibition of the sacral reflex arcs (the latter tending to produce micturition in response to stretching of the bladder) were little involved.

In discussing these cases, Dr. Robertson said that a certain unity was apparent in the histories reported. Each child had complete paralysis of both lower limbs. In addition to the myelitic lesion there was failure of vision, unilateral in one case and bilateral in the other, due to optic atrophy probably following optic neuritis. In the more severe case, in which the intercostal muscles also were more severely affected, signs indicating involvement of the medulla appeared after a short interval. In each case there was a strong tendency to improvement. The diagnosis of *neuromyelitis optica* was made when severe paraplegia was preceded or followed within a short space of time by failure of vision due to optic neuritis. Various statements had been made with regard to other points, the variations depending upon the small experience of any one author. In some cases no improvement occurred, but in others the vision and power were regained. It was usually said that relapses did not occur. Microscopic examination revealed patchy demyelination, chiefly around vessels, with perivascular infiltration of lymphocytes and fewer polymorphonuclear cells. When the lesion was severe, axis cylinders suffered destruction; when it was slighter, preservation of the axis cylinders allowed varying degrees of recovery. In the acute stages scavenger cells laden with debris were seen; in late stages glial proliferation had led to sclerosis.

Dr. Robertson went on to say that it would be seen that clinically and pathologically the condition was allied to other demyelinating diseases—multiple sclerosis, acute disseminated sclerosis or disseminated encephalomyelitis. A further similarity lay in the ineffectiveness of any form of treatment, for it seemed impossible by any means to alter the natural course of these diseases. Much discussion had centred upon the classification and aetiological individuality of such conditions, but no certainty existed. There was no knowledge of the underlying cause. Most believed that the lesion was an infection, but some authors suggested the possibility of degeneration or destruction by toxins. Unfortunately the pathological picture was not characteristic, for the reaction of the nervous system to infection might be indistinguishable from that which followed an acute destructive lesion of other causation. The frequency with which myelitis and optic neuritis occurred in close association producing a fairly constant clinical picture was the only justification for the term *neuromyelitis optica*. It was as if the clinical course of disseminated sclerosis was compressed within a short interval of time. It was possible that myelitis and optic neuritis might occur together as initial symptoms in a case of disseminated sclerosis, and if the condition was more than usually acute, it would resemble that in the cases under discussion. However, the frequent presence of relapse seemed to differentiate the condition in the cases under discussion, although sometimes only one eye was affected and relapses did occur. Upon this basis the condition in the second case would be better called acute disseminated sclerosis, in spite of the youthfulness of the patient, or disseminated encephalomyelitis with optic neuritis. The point was of some practical significance, for the prognosis was gloomier if the diagnosis was disseminated sclerosis.

Dr. H. BOYD GRAHAM said that the child had been referred to him from the Riverina, the relatives being in a state of

trepidation lest poliomyelitis might be the cause of his ailment. He felt certain, however, that if it was poliomyelitis it was an unusual variety of the disease. The child himself was free from pain and fear. He was weak on one leg and felt unsure on the other. This had produced a pronounced limp. He was free from cough, and afebrile. Dr. Graham said that he had made a note of the eye symptoms, which apparently manifested themselves on the journey to Melbourne. He was interested in Dr. Robertson's elucidation of the syndrome. Dr. Graham said that he recalled the case of a child, aged two years, who presented herself with paraplegia. She was apparently too young for eye symptoms to declare themselves. As she had helped herself to her father's hoard of tobacco and continued to pass tobacco for two weeks in the stools, it was presumed that this was the basis of her ailment. This child took seven or eight months to recover. In Dr. Robertson's case Dr. Graham had inquired about the possibility of such a toxic cause, but no tobacco was at hand in this instance. However, the scotoma and amblyopia fitted in with some such aetiological factor. Dr. Graham said that he had wondered also whether a neurotropic virus might be incriminated.

Dr. GUY SPRINGTHORPE thanked Dr. Robertson for his masterly presentation of the subject. The cases were unlike those of typical poliomyelitis, but in epidemics one had to eliminate as far as possible such a cause. This condition had originally been described by Dorik more than thirty years earlier, and only a few odd cases had appeared in the literature. Dr. Springthorpe recalled that most cases described had proved fatal usually in two or three months. Post-mortem findings were extensive demyelination in the cord and changes in one or both optic nerves. It was difficult to decide whether they were separate entities. Such cases were referred to as so-called *neuromyelitis optica* and regarded as of the same nature as acute disseminated encephalomyelitis. It was assumed that the cause was some neurotropic virus. Recovery of both these children made one wonder whether the lesion was a specific entity and whether these two children had not been fortunate to survive.

Dr. ROBERT SOUTHEY said that he felt they might be dealing with an atypical form of poliomyelitis. Both children had had some preceding febrile disturbance and had then developed signs in keeping with some virus infection.

Dr. MOSTYN POWELL said that he would not regard the children as suffering from atypical poliomyelitis. The lesions were fairly gross, and cases of such severity unassociated with headache or neck stiffness were extremely unusual. Moreover, in these cases the plantar reflexes were extensor in type, and signs of pyramidal involvement were also present.

Dr. J. B. COLQUHOUN said that in his experience, in a most amazing assortment of cases the original diagnosis had been poliomyelitis. One woman who had cared for a child suffering from poliomyelitis developed spastic ataxia. This would have been thought to rule out poliomyelitis, but she was sent to the Queen's Memorial Infectious Diseases Hospital, Fairfield. It was soon shown that she was spastic on one side of the body, and the diagnosis of disseminated sclerosis was made. A second patient whom Dr. Colquhoun remembered was a man who presented with transverse myelitis at the level of the second thoracic vertebra and a typical Brown-Séquard phenomenon below that level. Because of the epidemic, he too was sent to Fairfield, when a cursory examination would have revealed a tumour about the scapular region. A third patient diagnosed as suffering from poliomyelitis had a fracture in the neck of the humerus, and a fourth had foot drop from diabetic neuritis. Dr. Colquhoun said that it was therefore not surprising that poliomyelitis had been thought of in Dr. Robertson's cases. The presence of exaggerated deep reflexes should point in the opposite direction.

Dr. A. P. DERHAM said that the virus of poliomyelitis did not usually produce exaggerated reflexes, but there was no reason why it should not do so.

Dr. MURRAY CLARKE asked whether the visual changes observed in these cases had been described in early poliomyelitis.

Dr. Robertson, in reply, agreed that the lesion in the cases under discussion was not poliomyelitis, in which disease the anterior horn cells were attacked almost to the exclusion of the white matter. The presence of sensory loss, extensor plantar reflexes and optic neuritis was arrayed against this view. Tobacco poisoning was hard to exclude, but equally difficult to assert as a cause for the condition. The question of a virus origin for the disease was undecided,

and the literature was confused on the matter. Certain viruses did affect the white matter, of which that of rabies was an example. Vaccinal encephalomyelitis produced similar findings. It might be that the myelitis was stirred up by vaccination. Landry's myelitis was one in which the affection ascended the spinal cord.

(To be continued.)

Correspondence.

SEVERE LIVER DAMAGE IN INFECTIVE HEPATITIS.

SIR: In the journal of October 12, 1946, you published Douglas Stuckey's excellent account of a soldier who contracted hepatitis in the tropics. All who have seen similar cases will be interested in the details of the clinical notes. However, it is difficult to accept without reservation the author's opinion that the disease was infective in origin. Although Dr. Stuckey may have had some doubts about the aetiology, he does not appear to have stressed any alternative causal factors.

Now that the tumult is over, it is wise to discuss freely any possible cases of "Atebrin" intoxication which may have occurred during the war. This is not to deny the magnificent role of "Atebrin" in bringing victory, or to cast doubt on the justification for its use. But other and perhaps more suitable antimalarials are coming along, and it is therefore only right to try to evaluate any disadvantages of the drug.

As *The Lancet*⁽¹⁾ states, it has been fairly well established that "Atebrin" has a toxic action on the skin and produces an atypical lichen planus in a proportion of those who take the drug continuously for long periods. In animals, necrosis of the liver may result from large doses.⁽²⁾ Surely, then, it is not too much to expect that "Atebrin" may cause, if only extremely rarely, a toxic necrosis in human subjects. If Dr. Stuckey had made and elaborated upon this small concession, there could have been no cause for complaint.

Moreover, to help in evaluating such possible "Atebrin" toxicity, it would have been valuable if Dr. Stuckey had recorded whether the drug was continued after the diagnosis of hepatitis had been made.

Yours, etc.,

J. P. O'BRIEN, Pathologist.

Prince Henry Hospital,
Little Bay,
Sydney.

October 18, 1946.

References.

- ⁽¹⁾ *The Lancet*, December 1, 1945, page 711.
- ⁽²⁾ W. R. M. Drew and J. Reid: "Prolonged Administration of Mepacrine", *The Lancet*, July 28, 1945, page 107.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

COURSE IN ADVANCED MEDICINE AT SYDNEY.

THE Post-Graduate Committee in Medicine in the University of Sydney wishes to announce that a course in advanced medicine suitable for candidates for the M.R.A.C.P. examination will be conducted for a period of twelve weeks from January 13 to April 3, 1947, the fee for which will be £31 10s. The programme has been arranged to take place mainly in the afternoons, from approximately 2 to 5 o'clock p.m. on five to six days per week, and will include the following:

1. Four demonstrations in electrocardiography (normal cardiogram, coronary disease, the arrhythmias, deficiency diseases and infections).
2. Ward rounds to be held at the principal metropolitan hospitals approximately twice per week and to include demonstrations of cardio-vascular, nervous and chest disease *et cetera*.
3. Library seminars at which recent literature on set subjects will be discussed.

4. Set lectures on the more obscure medical, biochemical, physiological and pathological problems.

5. Demonstrations of the *fundus oculi*.

6. Demonstrations of pathology and hæmatology to be held in the pathological departments of the metropolitan hospitals.

7. Discussions on applied physiology.

8. Demonstrations of the application of radiological methods of diagnosis to medical diseases.

9. Demonstrations of psychiatric cases at Broughton Hall.

10. The exhibition of selected medical films, lantern slides, strip films *et cetera*.

11. Portions of the annual post-graduate course of interest to students in advanced medicine (lectures given by practitioners recently returned from overseas).

12. Library seminars in which students will participate.

It is expected that students will devote the whole of their time to study, and for this reason the mornings may be set aside for reading. Opportunity should be taken to peruse all the recent medical literature, and students will be guided in their reading by the supervisor of the course, Dr. Selwyn G. Nelson.

It is essential that candidates intending to take this course should make final arrangements with this committee at the earliest possible date. Those who are desirous of enrolling, but who cannot devote full time to study, should submit details of the time available to them to the committee for consideration.

Medical Prizes.

THE STAWELL PRIZE.

THE Stawell Prize, a memorial to Sir Richard Stawell, is open for competition. The amount of the prize is £30. The conditions are as follows:

1. The prize shall be awarded to the writer of the essay adjudged to be the best on a subject selected annually.
2. The subject for 1946 is "The Management of Diabetes Mellitus in Childhood".
3. The dissertation should be based on personal observation and experience of the writer.
4. The competition is open to graduates of any Australian university.
5. The trustees reserve the right to withhold the award.
6. Essays must be delivered to the Medical Secretary, British Medical Association (Victorian Branch), by 4 p.m. on November 30, 1946.
7. Each essay must be typewritten or printed and must not exceed 75,000 words in length.
8. Each essay must be distinguished by a motto and must be accompanied by a sealed envelope marked by the same motto, containing the name and address of the author.
9. The trustees reserve the right to publish the prize essay.

Obituary.

WALTER JOSEPH CRAIG.

WE regret to announce the death of Dr. Walter Joseph Craig, which occurred at Box Hill, Melbourne, on October 27, 1946.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Gray, John Benjamin, provisional registration, 1946 (Univ. Sydney), Marrickville District Hospital, Marrickville.

Clarke, Frederick George Joseph, M.B., 1943 (Univ. Sydney), Marlborough Hall, Roslyn Avenue, Roslyn Gardens.

THE undermentioned has applied for election as a member of the Tasmanian Branch of the British Medical Association:

Connard, Allan Barrie, M.B., B.S., 1946 (Univ. Melbourne), General Hospital, Launceston.

Corrigendum.

A LETTER has been received from Malaya from Mr. H. Fairfield Smith, Statistician, who contributed an addendum on the "Frequency of Detection of Cysts of Entameba Histolytica in Stools from Patients Apparently Recovered from Amebic Dysentery" to the paper by Major A. T. H. Marsden in the issue of June 29, 1946. He explains that the paper was written in Thailand and he did not see a copy of the typescript or of the printer's proof. He wishes to make the following corrections:

On page 917, at the foot of Table IV: for (5d.f.)=18.35 read $\chi^2(5d.f.)=18.35$. Tables II and III: for Percentage read Percentage of Positives, and under Total, 100 should be in the column headed Positive.

On page 918, Table VI: for Deviation = +34.5 read Deviation = 34.5.

On page 919, Table VIII: for V read v ; line 5: for r_k read n_k ; lines 7-12: read least one cyst in k specimens is $Q = .9999967^{(n_1 + n_2 + \dots + n_k)} \rightarrow .9999967^{kv}$, where v is the average number of cysts per day passed by the patient; and the probability of observing one or more cysts in k specimens is $P = (1 - Q)$. Table VIII shows P for $k=1$ to 60, and for $v=1,000$ to 1,000,000; line 17: for $P' = P_0/p$ read $P' = Pp'/p$; second last line: for F. E. Drion read E. F. Drion.

THE FEDERAL MEDICAL WAR RELIEF FUND.

The following contributions to the Federal Medical War Relief Fund have been received:

Victoria.

A. J. Day, £20.
J. T. Tait, S. J. Cuming, D. F. Lawson, J. A. Kennedy, W. J. Newing, £10 10s.
C. S. Wood, T. O. Sayle, A. S. Anderson (second contribution), £10.
W. J. R. Mabin, L. Langmore, R. P. Gurry, J. P. Horgan, £5 5s.
John F. Williams, R. K. Birnie, £5.
F. J. Williams, £2 2s.
Total: £135 12s.
Grand total: £15,303 19s. 6d.

Books Received.

"Aids to the Diagnosis and Treatment of Venereal Diseases", by T. E. Osmond, B.A., M.B. (Cantab.), M.R.C.S. (England), L.R.C.P. (London): 1946. London: Baillière, Tindall and Cox. 64" x 4", pp. 146. Price: 5s.

"Manual of Diagnostic Psychological Testing, II. Diagnostic Testing of Personality and Ideational Content", by David Rapaport, Ph.D., and Roy Schafer, B.S., with the collaboration of Merton Gill, M.D.: 1946. New York: Josiah Macy, junior, Foundation Publications. 9" x 6", pp. 106. Price: \$75.

"Renal Hypertension", by Eduardo Braun-Menéndez, Juan Carlos Fasciolo, Luis F. Lefoir, Juan M. Muñoz and Alberto C. Taquini; translated by Lewis Dexter, M.D.: 1946. Springfield, Illinois: Charles C. Thomas. 9" x 6", pp. 484, with illustrations. Price: \$6.75.

"Early Ambulation and Related Procedures in Surgical Management", by Daniel J. Leithauser, M.D., F.A.C.S.: 1946. Springfield, Illinois: Charles C. Thomas. 9" x 6", pp. 246, with illustrations. Price: \$4.05.

"Fundamentals of Immunology", by W. C. Boyd, Ph.D.: 1946. New York, Toronto: Staples Press Limited; London: John Bale Medical Publications Limited. 9" x 6", pp. 460, with illustrations. Price: 40s.

Medical Appointments.

Dr. J. P. Higgin has been appointed quarantine officer at Broome, Western Australia, under the *Quarantine Act*, 1908-1924.

Dr. D. J. C. Smythe has been appointed quarantine officer under the *Quarantine Act*, 1908-1924.

Dr. H. W. Fitzpatrick has been appointed to the Board of the Devon Public Hospitals District as representative of the medical practitioners residing and practising in the district under the provisions of *The Hospitals Act*, 1918, of Tasmania.

Diary for the Month.

- Nov. 12.—Meeting of Federal Council, British Medical Association in Australia, Adelaide.
Nov. 12.—Tasmanian Branch, B.M.A.: Ordinary Meeting.
Nov. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Nov. 13.—Victorian Branch, B.M.A.: Branch Meeting.
Nov. 14.—South Australian Branch, B.M.A.: Council Meeting.
Nov. 19.—New South Wales Branch, B.M.A.: Medical Politics Committee.
Nov. 20.—Western Australian Branch, B.M.A.: General Meeting.
Nov. 21.—Victorian Branch, B.M.A.: Executive Meeting.
Nov. 21.—New South Wales Branch, B.M.A.: Clinical Meeting.
Nov. 22.—Queensland Branch, B.M.A.: Council Meeting.
Nov. 26.—New South Wales Branch, B.M.A.: Ethics Committee.
Nov. 27.—Victorian Branch, B.M.A.: Council Meeting.
Nov. 28.—South Australian Branch, B.M.A.: Council Meeting.
Nov. 28.—New South Wales Branch, B.M.A.: Branch Meeting.
Dec. 3.—New South Wales Branch, B.M.A.: Organization and Science Committee.
Dec. 4.—Victorian Branch, B.M.A.: Branch Meeting.
Dec. 4.—Victorian Branch, B.M.A.: Council Meeting.
Dec. 4.—Western Australian Branch, B.M.A.: Council Meeting.
Dec. 5.—New South Wales Branch, B.M.A.: Special Groups Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phoenix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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